DEC 16 1924

Medical Lib.

BULLETIN

OF

THE JOHNS HOPKINS HOSPITAL

(THE PUBLICATION OF THE MEDICAL SCHOOL AND HOSPITAL)

(SUPPORTED BY THE DE LAMAR FUND OF THE JOHNS HOPKINS UNIVERSITY)

Vol. XXXV—No. 406] BALTIMORE, DECEMBER, 1924 [Price, 50 Cents

CONTENTS

	PAGE
An Experimental Study of the Anastomotic Circulation in the Dog. (Illustrated) By Frederick L. Reichert	385
Pernicious Anemia and Renal Insufficiency. By Ralph H. Major, M. D.	390
A Statistical Study of Eight Hundred and Eighty-eight Cases of Biliary Tract Disease. By Alfred Blalock, M. D.	391
The Effect of Intravenous Injection of Mercurochrome on the Kidneys. (Illustrated) By Justina H. Hill and Charles Y. Bidgood, M. D.	409
Note on a Timing Device for the Determination of the Refractory Period of the Heart. (Illustrated) By F. R. Dieuaide, M. D. and R. H. Turner, M. D.	411
Invitation to American Physicians	411
The Use of Plaster in the Treatment of Fractured Femurs. (Illustrated) By W. M. Fibor	412
The Formation of Bile Pigment from Haemoglobin in Tissue Cultures. By Arnold Rice Rich	415
William Wood Russell	416
The Isolation of Adenine Nucleotide from Blood. By William S. Hoffman	417
Notes on New Books	417
Books Received	420
Index to Volume XXXV of the Johns Hopkins Hospital Bulletin	421

Entered as Second-Class Matter at the Baltimore, Maryland, Postoffice.
Acceptance for mailing at special rate of postage provided for in Section 1103, Act of October 3, 1917. Authorized on July 3, 1918.

AN EXPERIMENTAL STUDY OF THE ANASTOMOTIC CIRCULATION IN THE DOG *

By Frederick L. Reichert

(From the Department of Surgery, the Johns Hopkins University)

In 1904, nearly twenty years before his death, Professor Halsted [1] became interested in the results which followed partial and complete occlusion of the abdominal aorta by ligatures and bands. In 1845, Luigi Porta [9] had demonstrated that the anastomotic circulation which followed the complete obliteration of the aorta in animals took place in part through vessels that he illustrated very well but did not identify (Fig. 2). Kast,[6] in 1879, emphasized the fact that the internal mammary and epigastric arteries were also important as indirect collateral channels. Later, some of Professor Halsted's experiments made him doubtful whether his own interpretation of Porta's anastomotic vessels was correct. Accordingly, he suggested a series of investigations to work out the details of the collateral circulation which develops after ligation of various large arteries.†

Of almost equal interest to him was the study of the changes which occurred in the main arterial trunks at the site of ligation. In this paper will be found an amplification of Professor Halsted's experiments which in a great measure confirm his predictions. Before proceeding with the details of the developing anastomotic circulation, I shall consider what happens to a vessel at the site of its occlusion.

Changes in an Artery after Ligation.—When a large artery is ligated, it gradually becomes obliterated from its proximal to its first distal branches. Ultimately, by a process of cell proliferation, the vessel is transformed into a fibrous cord. In a series of twenty-two experiments, undertaken to study these changes in the artery, the whole length of the vessel was explored at intervals after the ligation and the following observations were made.

If, immediately after a large artery has been tied, the vessel is punctured with a knife proximal to the ligature, blood will *spurt* from the wound; but when the puncture

* Received for publication on September 20, 1924.

† These experiments were begun in 1921 with the assistance of Dr. Charles Y. Bidgood.

is distal to the ligature, blood will only *slowly ooze*. If a branch of the artery intervenes between the ligature and the distal puncture the result is the same, i. e., there is only a slow ooze. On repetition of the above experiments 24 hours later the results are similar, except that, when the puncture wound is made beyond the first distal branch, the blood oozes briskly, or even has a slightly pulsating flow. This change is due to the collateral circulation which has now begun to develop through the first distal branch. After an interval of 3 or 4 weeks the flow of blood from a wound in the proximal segment is reduced to a small pulsating stream; in the distal segment there is no change until the first branch is passed, beyond which there is a small pulsating flow, very similar to that in the proximal segment.

Fifteen weeks after the ligation there is *no flow* of blood (though a drop of blood may exude) from either segment up to the first branch, but beyond this point the vessel pulsates strongly and there is a vigorous outflow of blood when its wall is punctured. In other words, at this time the lumen of the artery is practically obliterated up to its first proximal and first distal branches. This is complete before the fifth or sixth month, by which time the vessel has changed into a fibrous cord without pulsation and without any oozing when incised. As the above changes appear, there is a gradual diminution in the circumference of the artery, indicating a reduction in the size of its lumen.

The above observations hold true in all instances in the segment proximal to the ligature, but the findings distal to the ligature may be modified if the ligature is applied close to a bifurcation or trifurcation. In some instances it has been shown by Professor Halsted that the artery is not obliterated, but that a slight degree of dilatation occurs just distal to the ligature. The experiments of Professor Halsted [3] in 1916 seemed to demonstrate that after ligation of an artery there is a remarkable fall in blood pressure in what he termed the dead arterial pocket and that this lowered blood pressure is the immediate factor in the obliteration of the artery. When he completely occluded the aorta in dogs just above the trifurcation, in 3 out of 7 cases there was a slight degree of dilatation just distal to the ligature. Beginning dilatation distal to a ligature on the innominate artery appears in one of my animals (Fig. 8). The drawings of Luigi Porta (Fig. 2) show a pronounced dilatation of the aorta and its ventricle immediately below the site of ligation. The ligatures in the two dogs had been applied 8 and 15 months before the death of the animals. Professor Halsted felt that a dilatation of this ventricle-like portion of the aorta between the occluding band and the trifurcation might be expected in cases of complete occlusion, for the anastomosis is very free in this situation and the dead pocket is usually, perhaps always, too short to become obliterated.

The results of our experiments also confirm his view that "the intimal surfaces of arteries brought intact in apposition, whether by ligation or by band never, in my experience, have united. This statement will be received sceptically, for it is at variance with the quite universally accepted view that uncrushed intimal surfaces if brought gently in contact adhere and thus occlude the artery. . . . . The process of occlusion is, I believe, somewhat as follows: The death of the arterial wall having been brought about by the pressure of the band, a gradual substitution or organization of the necrotic tissue takes place, the new blood vessels penetrating it from both ends. The absorption of the lifeless wall proceeds coordinately with its vascularization or organization."

Vascular Injections with the Opaque X-ray Mass of Hill.—It was hoped that after vascular injections of a suitable roentgenographically opaque mass, stereoscopic X-rays would clearly demonstrate the new blood vessels which result from ligation of the abdominal aorta. This should disclose in graphic form the same vessels as those depicted by Porta, and presumed to be vasa vasorum.

In addition to its roentgenographic property, such an injection mass must not diffuse into the tissues, and yet must fill at least the finer arterioles without passing through the capillary bed. The only method which answered all of these requirements was that recently evolved by Eben C. Hill.[5] This we have used exclusively.*

The technique of the injections was as follows: immediately after sacrifice of the dog with ether, a cannula was introduced into the ascending arch of the aorta through the left ventricle. It is important that the sternum should be so divided in the midline as not to injure the internal mammary and intercostal arteries, which are often important as collateral channels. A suspension of 17 per cent bismuth oxychloride in 10 per cent acacia was slowly injected under a pressure of 140-150 mm. of mercury in puppies, and 170-240 mm. Hg. in adult animals. With these pressures, controlled by observing whether the mass had penetrated the anterior ciliary arteries, extravasations were avoided, and the vessels were distended to about their normal size. Following the injection, the abdominal viscera (with the exception of the kidneys) were removed in order to avoid obscuring the parietal vessels. Stereoscopic x-ray plates were then taken immediately, the exposures being made especially for the soft tissues rather than the bony framework. In this way the arterial tree was clearly defined and gave a comprehensive idea of the distribution and relative location of the arteries and their branches, and the anastomoses.

As controls, the vascular system was studied in like manner in normal animals of the same ages. Photographs

* I am greatly indebted to Dr. Hill for his kindness in permitting unrestricted use of his newly discovered injection mass almost three years before publication.

of these injections are shown in Figs. 1 and 7. The labels are in accordance with the nomenclature used in Ellenberger and Braun's *Anatomie des Hundes*. Fig. 1 shows the main arterial system in the posterior half of a young dog. The abdominal aorta terminates in three large branches. Just above this trifurcation, between the 6th and 7th lumbar segmental arteries, a pair of vessels, the circumflexae iliacae profundae or abdominales, course in the abdominal wall. Their terminal arborations normally anastomose (*3*, Fig. 3), with another pair which arise just below the diaphragm—the phrenico-abdominales (*2*, Fig. 3). In most of the figures the lines of the deep epigastric and internal mammary arteries are faint because they are farther from the x-ray plate.

Vascular Injections after Ligation of the Abdominal Aorta.—The abdominal aorta can be ligated without danger of gangrene. In discussing the danger of gangrene from ligation of various large arteries, Professor Halsted [2] stated that "there is abundant evidence in support of the view that, in a general way, the larger the artery or the nearer it is to the heart, the less impairment of the circulation attending its ligation. . . . Peripheral gangrene has not been observed in consequence of ligation of the aorta. It may occur after ligation of the common iliac; has occurred much more frequently after ligation of the external iliac, and has followed ligation of the popliteal artery in a considerable percentage of cases." In offering the generally accepted explanation of this imperfect law Kümmell [7] wrote as follows: "It seems natural, within certain limits, that the nearer the ligated vessel is to the central organ of the circulation, the easier it is for the collateral routes, by means of the increased pressure from the heart, to develop."

In ten of our series of experiments, six with ligation and four with ligation followed by division of the abdominal aorta proximal to the trifurcation, the pulsation in the femoral artery could not be felt immediately after operation, but it returned in from four to six weeks. In these studies young dogs were used, since adult animals not infrequently show evidence of spinal cord changes.

That some degree of collateral circulation is normally present is shown in Fig. 3, which illustrates the aorta injected with bismuth immediately after its ligation and division. One can make out the mass in the three branches and well down into the legs. Although only the main trunks are outlined, one can see at least two points of anastomosis, the third being between the superior and inferior epigastric arteries; this last point could be demonstrated with stereoscopic vision though it could not be distinctly shown in the photograph. The anastomosis between the phrenico-abdominalis and circumflexa iliaca profunda vessels is quite evident, as well as that between the terminal branches of the lumbar arteries.

In contrast to the normal collateral circulation (Fig. 3), that shown in Fig. 4, where the injection was made 12 days after division of the aorta, shows a complete filling of the vessels distal to the ligature. In Fig. 4 the anastomosis between the superior and inferior epigastric arteries is labeled *1*. The collaterals between the separated lumbar segmental arteries are not prominent at this stage. A well developed communication exists between the phrenico-abdominalis and circumflex iliac profunda vessels (*3*, Fig. 4). The anastomosis is shown between the circumflexa iliaca profunda and branches of the circumflexa femoralis lateralis (*4*, Fig. 4), as well as a smaller anastomotic route between the circumflexa iliaca profunda and branches of the a. femoralis anterior (*5*, Fig. 4).

If, instead of making our usual complete injection of the arterial system, the bismuth mass be put into the aorta immediately above the ligature, an entirely different picture of the vascular system caudal to the ligation is disclosed. Such an injection fails to take into account the great importance of the epigastric vessels as collateral channels which can be shown by a subsequent injection through the heart. After the latter injection the plates reveal a complete filling of the vessels of the posterior limbs, owing to the passage of the mass through the internal mammary into the inferior epigastric arteries.

The roentgenograms, taken when only the descending aorta just proximal to the ligature was injected, show the small size and incomplete filling of the trifurcating branches as well as the poor injection of the posterior extremities. During this injection the vessels were observed through the abdominal opening. While slowly injecting the mass, we could readily see the filling of the arteries distal to the ligature through the individual collateral routes, the bismuth first appearing in the vessels of the mesentery and small intestine. With a slightly increased pressure, the injection mass appeared in the aorta immediately distal to the ligature, entering the branches of the trifurcation through the adjacent lumbar segmental vessels. Finally, the injection fluid approached the ligated area from the distal portion of the external iliac arteries; in other words, there was a retrograde flow toward the trifurcation, until finally the trunks distal to the ligature were filled but not distended with the suspension. The anastomoses in the posterior abdominal wall were distinctly seen between the circumflexa iliaca profunda and the circumflexa femoralis lateralis. As the inferior epigastric arteries filled their small branches whitened and the bismuth eventually passed into the superior epigastric tree.

The great wealth of collateral channels present six months after division of the aorta is beautifully shown in Fig. 5. The print bears a close resemblance to the drawings of Luigi Porta, but in none of the injections were any vasa vasorum demonstrable. These small arteries, as drawn by Porta and at first erroneously interpreted by

Prof. Halsted, seem rather to be newly formed anastomotic vessels between the greatly enlarged lumbar segmental arteries. While some of these vessels appear to spring from the aortic stump, in reality they are branches of the lumbar segmental arteries, and have become nearly straight channels as the result of the retraction of the divided ends of the aorta.

In two of the animals the whole posterior wall was removed in a block and cleared by the Spalteholz method. In this way the opaque arteries and the network of collateral vessels were boldly revealed supported in a transparent tissue. Neither in this manner nor by the roentgenographic stereoscopic plates were any vessels seen that could be interpreted as vasa vasorum.

In this figure, as in the others, many of the finer arterioles and capillaries which were distinct in the stereoscopic plate have been lost in the making of the print. Some of the larger vessels have been retouched before reproduction, but no attempt was made to trace into the photograph any of the amazing network of tiny arterioles.

Results of Vascular Injections After Other Ligations in the Posterior Half of the Body

After Ligation at the Trifurcation.—Ligation separately of each branch of the trifurcation—that is, ligation of the right and left external iliac, the right and left epigastric, and the medial sacral arteries at their origin,—results in an entirely different x-ray picture. None of the main trunks contain bismuth, yet all the smaller vessels in the limbs are filled just as completely as after division of the aorta a short distance above the trifurcation. In places, portions of the main trunk are seen but no arboreal system is to be distinguished. Three important points of anastomosis follow this type of ligation: (1) between the superior and inferior epigastric arteries; (2) between the last two lumbar segmentals and the ilio-lumbalis and circumflex femoralis lateralis vessels; and (3) between the superior gluteal and the lower lumbar arteries.

After Ligation of the External Iliac and Hypogastric Arteries.—Following ligation of the right external iliac and hypogastric arteries, the collateral circulation is established between (1) the circumflexa iliaca profunda and the branches of the anterior femoral artery; (2) the right seventh lumbar and the iliolumbalis as well as branches of the anterior femoral artery; and (3) the terminal branches of the arteria ischiadica glutea inferior and the a. femoralis posterior media.

After Ligation of the External Iliac Artery.—Ligation of the external iliac artery on one side gives as complete an injection of the hind leg as the normal injection on the other side. The inferior epigastric artery is enlarged; there are anastomoses between (1) the a. femoralis posterior media and superior with the a. ischiadica s. glutea inferior; (2) the a. ischiadica s. glutea superior and branches of the femoralis profunda; (3) the circumflexa iliaca profunda and the circumflexa femoralis lateralis; and (4) the femoralis profunda and iliolumbalis.

Replantation of Thigh after Ligation of the Femoral Artery and Vein.—In another study, undertaken to determine the degree of swelling following division of the vessels and lymphatics of a limb, the thighs of several dogs were practically severed and the divided structures then united with sutures. A complete circular incision was made through the middle third of the thigh, dividing skin, subcutaneous tissue and muscles transversely. Only the femur, the sciatic and anterior crural nerves, and the femoral artery and vein were left intact. These remaining structures were carefully isolated and denuded of all areolar tissue to insure complete severance of all lymphatics. The extremity, which had thus been practically amputated, was replanted by carefully approximating the muscle stumps and skin edges. These replanted limbs united without infection and in no instance was there any evidence of gangrene.

This series showed one unusually interesting case. The left thigh (left side of Fig. 6) was replanted over 8 months before the animal was sacrificed and healed by first intention. Ten days later the right femoral artery and vein were ligated just below the femoralis profunda artery. Sixteen days before the dog was sacrificed the right thigh was replanted. The previous ligation of the femoral artery and vein had been overlooked, and at the operation they were found to have become converted into fibrous cords. Regretting that the function of these vessels had not been determined, we removed a portion of each nine days later. The artery was represented by a very small cord, with no pulsation, and when pricked it did not bleed. Sections of the artery showed the lumen completely obliterated and the vessel changed into a solid strand of fibrous tissue. The replantation was successful on the right side notwithstanding the fact that the femoral artery and vein had been ligated below the profunda branch 8 months previously. X-rays of the injected vessels taken 16 days after replantation on the right side show an absence of the femoral artery beyond the circumflex femoralis lateralis branch, and after the ligation its circulation had been assumed by the lesser vessels to the thigh. It is astonishing that healing progressed unhindered, since, superimposed upon the disturbance of circulation resulting from division of all the tissues down to the bone, the blood supply of the leg was presumably completely isolated by the ligation of the main artery and vein. Fig. 6 shows that the circumflexa femoralis interna has become a large vessel skirting close to the femur; possibly it had not been divided. The terminal branches of the a. ischiadica glutea inferior had increased and enlarged, as had also the muscular branches of the a. anterior femoralis. New arterial vessels had grown across the field of operation, forming numerous

anastomoses. The nutrient artery of the femur and possibly the circumflexa femoralis interna artery were the only connecting links of the vascular system after replantation. The fact that the femoral vein was ligated with the artery may have been a material factor in maintaining the life of the limb.

The importance of ligating the correspondingly named vein when the artery is injured, in order to minimize the danger of gangrene, was strongly emphasized by Sir George Makins [3] during the war. Prof. Halsted [4] quoted him as follows: " . . . . On these and other grounds it must be admitted that the balance of the collateral circulation is likely to be more efficiently maintained if the vessels which carry it on more nearly correspond in size and consequent equality in the blood pressure and rate of flow. The elimination, in fact, of the capacious main vein is a real advantage, since this for the time affords a too ready channel of exit for the diminished arterial supply, as well as an undesirable reservoir for stagnation." Prof. Halsted goes on to state: "We are compelled, I believe, to subscribe to the view that some degree of equilibrium of the arterial and venous systems must be maintained. Granting this, there vanishes any difficulty that there may have been in accounting for the very high percentage of gangrene observed to follow ligation of the artery in cases of arterio-venous fistulae. There is in these cases not only a great enlargement of the venous bed, but also a curtailment of the arterial tubage—a shrinkage or hypoplasia of the arteries distal to the fistula. Thus even before the artery is ligated the limb is handicapped by this lack of balance. When, now, the artery above a fistula is tied, irrigation with arterial blood is suppressed on one side of the capillary bed and on the other side of it the mixed blood is deprived of a share of the pressure by virtue of which the life of the limb was partially sustained."

Vascular Injections Following Ligations in the Anterior Half of the Body

The arterial system in the anterior half of the dog is shown in Fig. 7. Besides the origin of both carotid arteries from the innominate, the fifth right intercostal in the dog is usually the common trunk for the third and fourth and frequently for the second intercostals; the first, or a. intercostalis suprema arises from the truncus costocervicalis, a branch of the subclavian. The photographs show the heart faintly outlined, and the cannula in the arch of the aorta.

After Ligation of the Innominate Artery Just Distal to the Origin of the Left Carotid Artery.—The innominate artery was ligated in three animals; in each the radiographic findings were identical. The vessel was exposed through a thoracic approach, and a ligature of heavy silk was placed just beyond the origin of the left carotid artery. An injection made 4 months after this ligation (Fig. 8) shows the development of numerous collateral vessels in the upper thoracic region; those between the terminal branches of the internal mammary and the inferior epigastrics are quite prominent. A large anastomosis (*3*, Fig. 8) exists between the intercostalis suprema of the subclavian system and the right fifth intercostal trunk through the second, third, and fourth intercostals. A third place of anastomosis is between the posterior muscular branches of the right sixth intercostal (*8*, Fig. 8) on the one hand, and the several branches of the subclavian. This sixth intercostal artery has enlarged and its branches form at least four different anastomotic channels: that is, there are collateral branches between it and the a. transversa scapulæ, a branch of the truncus omocervicalis (*4*, Fig. 8); between it and the a. circumflexa scapulæ, a branch of the subscapular artery (*6*, Fig. 8); between it and the artery thoraco-dorsalis, another branch of the subscapular (*5*, Fig. 8); and finally it forms a communication with branches of the a. brachii profunda (*1*, Fig. 8). Another collateral route is through the right cervicalis profunda artery, which sends branches across to the corresponding artery on the other side (*2*, Fig. 8). A coarse network of small vessels makes the communications between the segmental branches of the vertebral arteries. It is interesting to note that the vessels distal to the point of ligation are of smaller calibre, especially the carotid and the internal mammary arteries, and to observe also the ventricle-like dilatation of the subclavian artery just distal to the ligature.

After Ligation of the Left Subclavian and Left Carotid Arteries.—The injections in Fig. 9 were made four months after the left carotid and left subclavian arteries had been ligated at their points of origin. Distal to the ligature the left common carotid artery is not outlined in bismuth, although beyond the superior thyroid branch the internal carotid vessel becomes visible. Dissection showed that the carotid artery between the point of ligation and the first distal branch had been converted into a fibrous cord. Both vertebral arteries are of about the same calibre, with a heavy segmental anastomosis all along their course, whereas the left internal mammary artery, which arises near the vertebral artery and has but few branches, is considerably smaller than the right. The upper intercostals are much larger than normal. The third and fourth intercostals form an enlarged trunk with a network of collaterals to the left intercostalis suprema (*2*, Fig. 9) and to the transverse scapular branch of the truncus omo-cervicalis (*3*, Fig. 9). The seventh left intercostal, besides being dilated, has a large lateral branch which courses upward in the axillary region to make a prominent anastomosis with the thoraco-dorsalis and the circumflex scapularis arteries (*4*, Fig. 9). This is the only plate in which a sudden change in the calibre of the thoracic aorta has been seen. No satisfactory explanation can be offered for this transition.

SUMMARY

The changes which occur in the large arteries at the site of ligation are described.

An effort has been made to define the collateral channels which develop after ligation of the main arterial trunks in the dog. Skiagrams have been taken of the vascular beds, injected with the opaque x-ray mass of Hill, at varying intervals after the ligation.

It has been shown that after division of the abdominal aorta, these collateral channels are not vasa vasorum, but are probably newly formed vessels.

BIBLIOGRAPHY

1. Halsted, W. S.: Partial, progressive and complete occlusion of the aorta and other large arteries in the dog by means of the metal band. Jour. of Exp. Med., 1909, XI, 381.

2. *Idem:* The effect of ligation of the common iliac artery on the circulation and function of the lower extremity. Johns Hopkins Hosp. Bull., 1912, XXIII, 65.

3. *Idem:* An experimental study of circumscribed dilation of an artery immediately distal to a partially occluding band, and its bearing on the dilation of the subclavian artery observed in certain cases of cervical rib. Jour. of Exp. Med., 1916, XXIV, 276-278.

4. *Idem:* On ligation of the left subclavian artery in its first portion. Johns Hopkins Hosp. Rep., 1920, XXI, 23.

5. Hill, E. C.: Notes on an opaque X-ray mass. Johns Hop. Hosp. Bull., 1924, XXXV, 218.

6. Kast, A.: Die Unterbindung der Bauchaorta. Ztschr. f. Chir., 1880, XII, 405.

7. Kümmell, H.: Die Unterbindung der Arteria iliaca communis. Arch. f. klin. Chir., 1884, XXX, 67.

8. Makins, Sir George: Gunshot injuries of the blood vessels. 1909, 8th Amer. ed., N. Y., Wood.

9. Porta, Luigi: Delle alterazioni patologiche delle arterie per la legatura e la torsione. Milano, 1845, pp. 350, 351, Plate V.

PERNICIOUS ANEMIA AND RENAL INSUFFICIENCY*

By RALPH H. MAJOR, M. D.

(From the Department of Internal Medicine, the University of Kansas School of Medicine, Kansas City)

The occurrence of albuminuria with a urine of low specific gravity in pernicious anemia has been noted by several observers. Coupland [1] in 1898 described a fixed specific gravity of the urine in this disease. Cabot [2] found albuminuria in 46 per cent of 506 cases of pernicious anemia and other observers have found that from 40 to 50 per cent of these patients show albumin in the urine.

These urinary findings have led to a study of the renal function in pernicious anemia by Christian,[3] Mosenthal,[4] Mosenthal and Lewis [5] and Tileston and Comfort.[6] A fixation of the specific gravity by the Mosenthal test was described by Christian,[3] Mosenthal [4] and by Stieglitz.[7] These observers regard the results as direct evidence of renal impairment. Christian believed that if the anemia persisted for a long time permanent renal impairment might occur, and Stieglitz suggests that the renal impairment may be due to a deposit of iron in the convoluted tubules of the kidneys.

It is interesting to note that Christian, Mosenthal and Stieglitz found the excretion of phenolsulphonephthalein normal but considered the results of the Mosenthal test as evidence of renal impairment. Kahn and Barsky [8] found "the renal function normal, as evidenced by the phenolsulphonephthalein test and the blood nitrogen partition," and many other observers have reported studies of the blood chemistry in pernicious anemia which do not suggest the presence of kidney disease. These results cause one to question whether there is a true renal impairment in pernicious anemia, while granting that a certain percentage of patients with pernicious anemia show the lesions of chronic nephritis at autopsy.

In a recent small series of patients, examination of the urine showed such a low excretion of chlorides as to suggest a retention. These patients were then given salol-coated sodium chloride tablets in doses varying from 6 grams to 20 grams per day. These observations were made upon five patients, in three of whom the data are sufficiently extensive to make the results of some value.

All of these patients were undoubted cases of pernicious anemia with a gastric anacidity, a high color index, a high volume index and a typical clinical appearance. The results of these observations are shown in Table I.

In these three patients the addition of large amounts of sodium chloride to a constant diet produced no increase in the excretion of the chlorides. They had no evidence of renal disease and two of the three had no albuminuria.

These findings suggest the possibility that the retention of chlorides in pernicious anemia is not due to renal disease but bears some analogy to the retention seen in lobar pneumonia and in certain cases of intestinal obstruction. In the latter condition Haden and Orr [9] have suggested that the retention of chlorides may be a protective mechanism and that the chlorides have a detoxifying action. Further extension of these observations in pernicious anemia is desirable to determine whether this retention of chlorides is a constant phenomenon and a protective mechanism.

* Received for publication August 14, 1924.

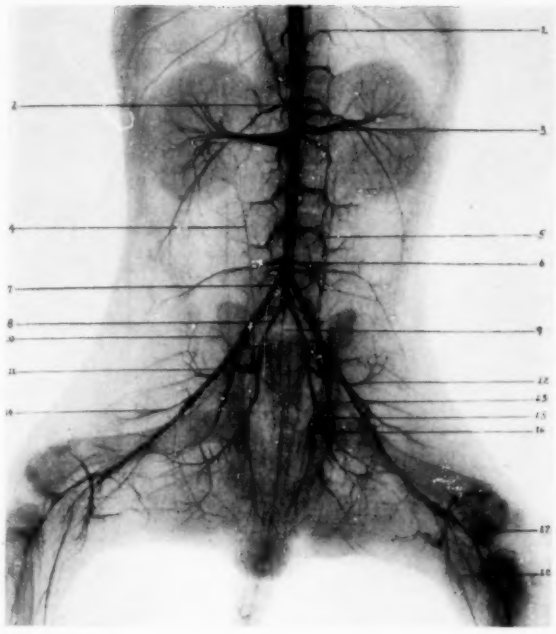


Fig. 1.—Normal arterial injection with Hill's opaque x-ray mass through arch of aorta. Posterior half of body. 1. A. lumb. I. 2. phren. 3. ren. 4. epigastr. 5. lumb. V. 6. circumfl. iliaca prof., or A. abd. 7. fem., or A. il. ext. 8. hypog. 9. sacr. med. 10. ili.-lumb. 11. isch. s. glut. inf. 12. circumfl. fem. ext. s. lat. 13. fem. prof. 14. musc. of a fem. ant. 15. isch. glut. inf. 16. prof. int. 17. popl. 18. tib. ant.

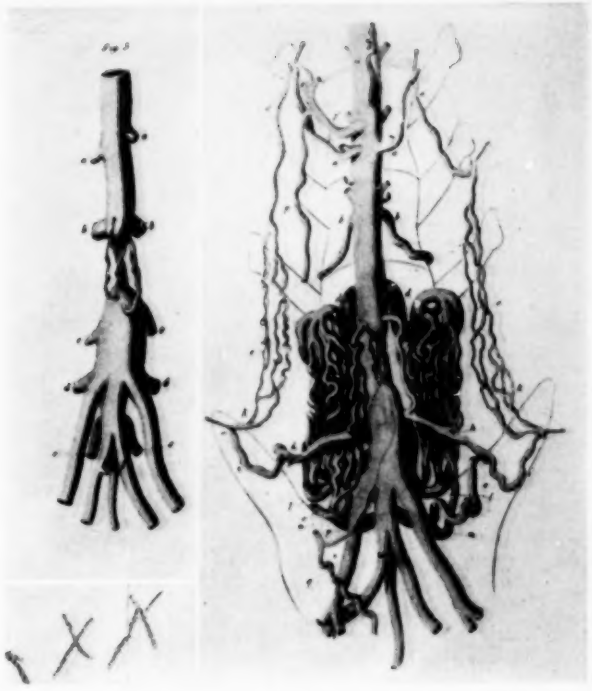


Fig 2.—From Luigi Porta, Plate V, *Fig. 3* (left) and *Fig. 5* (right). *Fig. 3.* Abdominal aorta of a dog ligated 8 months previously, with the direct anastomosis and the stumps of the lateral vessels, which formed the indirect anastomoses. *Fig. 5.* Abdominal aorta of a dog, ligated 15 months previously, with the entire anastomotic system between the stumps. Aorta dilated distal to the site of ligation.

Fig. 3.—Arterial injection immediately after division of abdominal aorta, showing collateral channels normally present. 1. A. ren. 2. phren.-abd. 3. circumfl. il. prof.

Fig. 4.—Arterial injection 12 days after division of abdominal aorta 1. anastomosis between inf. and sup. epigastric arteries. 2. A. lumb. V. 3. Anast. between A. phren.-abd. and A. circumfl. il. prof. 4. between A. circumfl. iliaca prof. and branches of circumfl. fem. lat. 5. between A. circumfl. il. prof. and branches of A. fem. anterior.

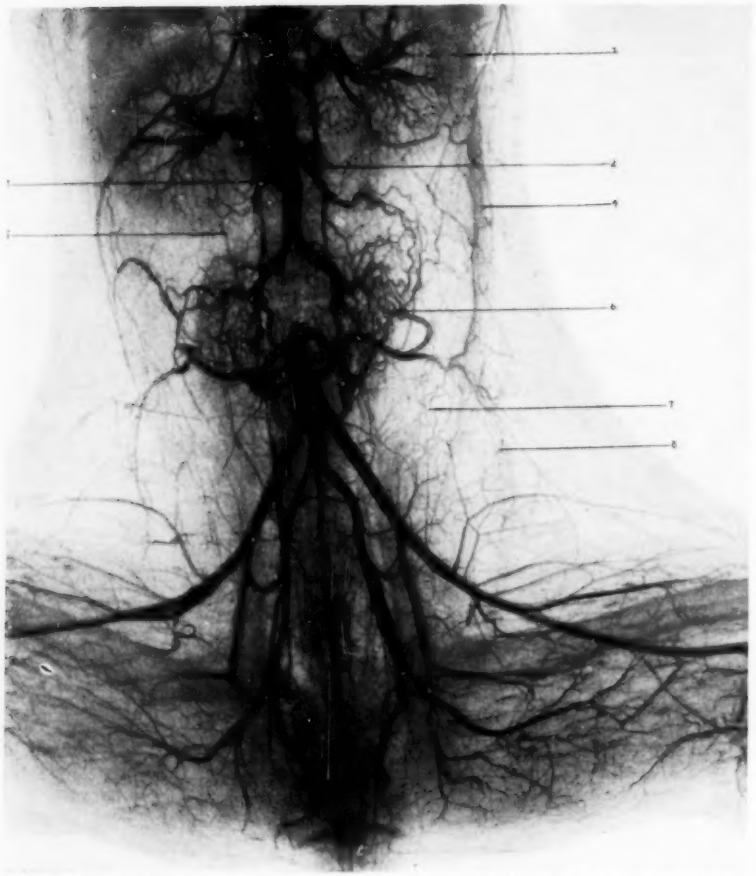


Fig. 5.—Arterial injection 6 months after division of abdominal aorta. 1. Terminal vessels in renal cortex. 2. A. lumb. IV. 3. Prox. stump of divided aorta. 4. Anast. between A. phren.-abd. and A. circumfl. il. prof. 5. Branches of inferior epigastric to anastomose with A. sup. epigastric. 6. Anast. between AA. lumb. V and VI. 7. between A. circumflexa iliaca prof. and A. il.-lumb. 8. between A. circumflexa il. prof. and A. circumflexa femo. lat.

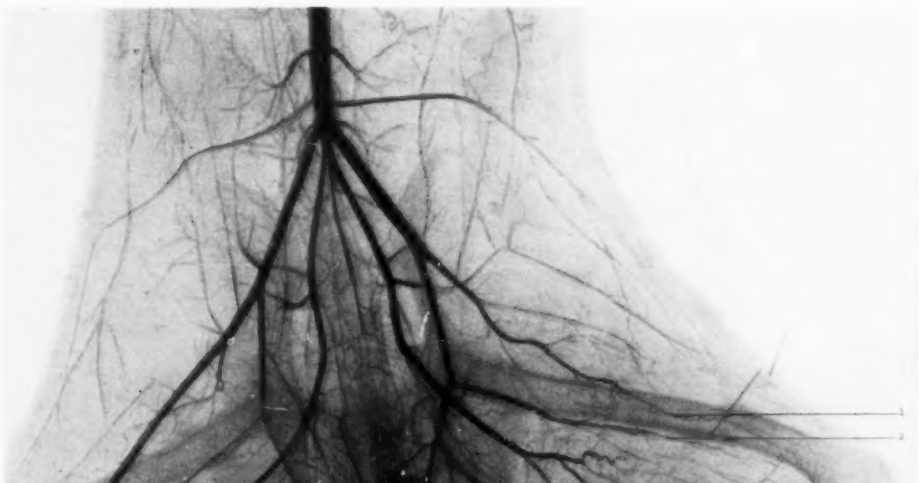


Fig. 6.—Arterial injection 8 months after ligation of right femoral artery and vein; 16 days after replantation of right thigh; 8 months after replantation of left thigh. 1. Nutrient artery of femur. 2. A. circumfl. fem. int., a branch of A. fem. prof.

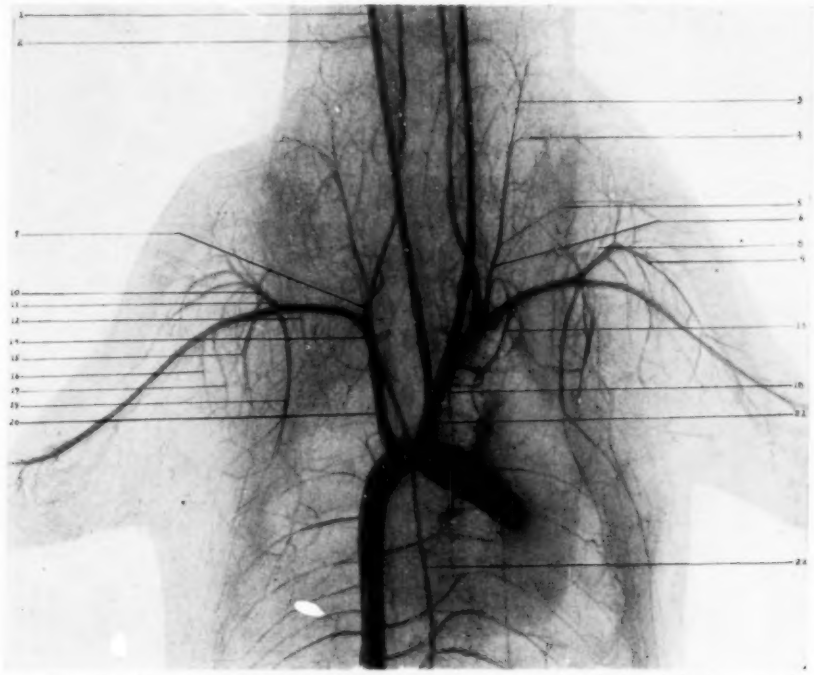


Fig. 7.—Normal arterial injection in dog of anterior half of body. 1. A. carotis d. 2. vert., ramus musc. 3. cerv. sup. 4. acrom. 5. scap. med. 6. cerv. asc. 7. Trunc. omo-cerv. 8. circumfl. hum. post. 9. circumfl. hum. ant. 10. circumfl. hum. 11. subscapu. 12. mamm. ext. 13. transv. scap. 14. Trunc. costo-cerv. 15. circumfl. scap. 16. brach. ant. 17. prof. brach. 18. intercost. supr. 19. thorac.-dors. 20. subcl. sin. 21. anon. 22. mamm. int.

Fig. 8.—Arterial injection 4 months after ligation of innominate artery just distal to origin of left carotid artery. 1. Segmental branches of A. verteb. 2. Anasto. between A. cerv. prof. s. and d. 3. between A. intercost. sup. and trunk of A. intercost. V dex. 4. between post. musc. branch of VI intercost. and A. transv. scap. 5. between post. musc. branch of VI intercost. and A. thorac.-dors. 6. between post. musc. branch of VI intercost. and A. circumfl. scap. 7. between post. musc. branch of VI intercost. and branches of A. prof. brach. 8. between post. musc. branches of VI intercost. and branches of A. subcl. 9. A. mamma. int. sin.

Fig. 9.—Arterial injection 4 months after ligation of left subclavian artery and left carotid artery. 1. Segmental branches of A. vertebr. 2. Anastomosis between III and IV intercost. and A. intercost. supr. sin. 3. between III and IV intercost. and A. transv. scap. 4. between lat. branches of VII intercost. and A. thor.-dors. and A. circumfl. scap. 5. Prox. stump of left carotid artery.

TABLE I.

L. H. Aged 58	E. F. Aged 41	T. E. Aged 53
R. B. C. 992,000	R. B. C. 2,592,000	R. B. C. 1,480,000
W. B. C. 5,000	W. B. C. 8,250	W. B. C. 3,050
Hb. 28 per cent (gasometric)	Hb. 62 per cent (gasometric)	Hb. 46 per cent (gasometric)
Color index 1.36	Color index 1.31	Color index 1.53
Volume index 1.38	Volume index 1.31	Volume index 1.53
Dec. 19..... 1.6 gm.	Nov. 16..... 1.4 gm.	Dec. 20..... .4 gm.
Dec. 20..... 1.3 gm.	6 gm. NaCl daily	Dec. 21..... .9 gm.
Dec. 21..... 2.3 gm.	Nov. 17..... 1.0 gm.	10 gm. NaCl daily
Dec. 22..... 1.8 gm.	Nov. 18..... 1.2 gm.	Dec. 22..... 2.0 gm.
Dec. 23..... 1.7 gm.	Nov. 19..... 1.6 gm.	Dec. 23..... 0.5 gm.
Dec. 25..... 1.8 gm.	Nov. 20..... 0.7 gm.	Dec. 24..... 0.8 gm.
6 gm. NaCl daily	Nov. 21..... 1.9 gm.	Dec. 25..... 6.0 gm.
Dec. 26..... .7 gm.	Nov. 22..... 0.2 gm.	
Dec. 28..... .9 gm.		
Dec. 29..... 1.0 gm.		
Dec. 30..... 1. gm.		

BIBLIOGRAPHY

1. Coupland, Sidney: *in* Albutt's System of Medicine, 1898.
2. Cabot, R. C.: *in* Osler and McCrae's Modern Medicine 1906, IV, 628.
3. Christian, H. A.: Renal Function in Anemia, Arch. Int. Med., 1916, XVIII, 429.
4. Mosenthal, H. O.: Renal Function as Measured by the Elimination of Fluids Salt and Nitrogen and the Specific Gravity of the Urine, Arch. Int. Med., 1915, XVI, 733.
5. Mosenthal, H. O. and Lewis, D. S.: A Comparative Study of Tests for Renal Function, J. A. M. A., 1916, LXVII, 933.
6. Tileston, W. and Comfort, C. W.: The Total Non-Protein Nitrogen and the Urea of the Blood, etc., Arch. Int. Med., 1914, XIV, 620.
7. Stieglitz, Edward J.: Disturbances of Renal Function in Pernicious Anemia, Arch. Int. Med., 1924, XXXIII, 58.
8. Kahn, Max and Barsky, Joseph: Studies on the Chemistry of Pernicious Anemia, Arch. Int. Med., 1919, XXIII, 334.
9. Haden, R. L. and Orr, T. G.: Use of Sodium Chloride in Treatment of Intestinal Obstruction, J. A. M. A., 1924, LXXXII, 1115.

A STATISTICAL STUDY OF EIGHT HUNDRED AND EIGHTY-EIGHT CASES OF BILIARY TRACT DISEASE

By ALFRED BLALOCK, M. D.

(From the Department of Surgery, The Johns Hopkins University and Hospital)

This clinical study includes every case with a diagnosis of disease of the biliary tract in the Surgical Service of the Johns Hopkins Hospital from its opening in 1889 up to January, 1924. During that period some 60,000 patients have passed through this service, and of these, 888 or 1.5 per cent had some disorder of the biliary tract.

The classification of these cases is based mainly on the presence or absence of stones and the position of the stones when present. It is thought that this type of grouping is less subject to error than that in which the cases are considered, respectively, as acute or chronic. The six groups into which these cases are divided are:

(1) Stones in the gall-bladder or cystic duct or both ..... 460 cases
(2) Stones in the common duct regardless of the location of other stones..... 139 cases
(3) Acute or chronic cholecystitis without the presence of stones ..... 136 cases
(4) Malignancy of some part of the biliary tract regardless of the presence or absence of stones ..... 42 cases
(5) Diagnosis of disease of the biliary tract; but no operation ..... 100 cases
(6) Miscellaneous group: Pericystic adhesions without evidence of disease of the tract itself (8 cases); Stricture of one or more of the ducts (3 cases) ..... 11 cases

Total..... 888 cases

These cases have been studied from the standpoints of (1) etiology, (2) symptoms, (3) physical examination, (4) laboratory tests, (5) operation and re-operation, (6)

bacteriology and pathology, (7) course immediately after operation and (8) ultimate result.

For the sake of brevity, the first 3 groups—patients operated upon for stones or for cholecystitis without stones—will be considered together.

Etiology, Race and Sex.—Table I shows a predominance of white over colored patients (32:1), whereas the ratio of all white to colored surgical patients is 5:1.

The proportion of females to males in these three groups combined is 2:1, whereas there have been more than twice as many males on the surgical service.

It is interesting that in the group without stones the male and female patients are about equal in number.

TABLE I.

Relation of race and sex to case distribution.

Group	Number of patients	RACE		SEX	
		per cent white	per cent colored	per cent male	per cent female
Stones in G. B...	460	97	3	28	72
Stones in C. D...	139	95	5	34	66
Without stones .	136	97	3	47	53
Total	735	97	3	33	67

Age.—The ages according to decades are given in Table II. They run fairly parallel for the three groups except that the patients in the group without stones, on the whole, are slightly younger—the youngest patient with gall-bladder disease without stones was eleven, while the youngest in the other two groups was eighteen years old. The average age was 44 years and more than half of the total number of patients were between the ages of 40 and 60. The age was not given in ten cases.

TABLE II.

Relation of age to case distribution.

Decade	Stones in G. B. Number of patients	Stones in C. D. Number of patients	Without stones Number of patients	Total number of patients	Per cent in decade
2nd	4	1	6	11	1.5
3rd	64	9	16	89	12
4th	122	28	45	195	27
5th	139	39	45	223	31
6th	90	39	17	146	20
7th	31	15	7	53	7
8th	5	2		7	1
9th	1				
Total	456	133	136	724	100

Typhoid Fever.—We find that 28 per cent of these patients had had typhoid fever (Table III), the highest percentage being in the group without stones. Typhoid antedated entry to the hospital by more than 5 years in 76 per cent of all patients. It is interesting that a larger number in the group without stones either had typhoid on entry or shortly preceding it. Of the 37 patients that had had typhoid fever in the common duct group, 26 had had it more than 20 years before admission.

TABLE III.

Relation of typhoid fever to case distribution.

Groups	No. of pts. with note	No. with preceding typhoid	Percentage with typhoid	TIME PRECEDING ENTRY			
				Less than 1 yr.	1 to 5 yrs.	5+ years	Time doubtful
Stones in G. B...	446	111	25	9%	11%	80%	4 pts.
Stones in C. D...	133	37	28	3%	22%	75%	
Without stones..	133	52	40	18%	14%	68%	2 pts.
Total	712	200	28	10%	14%	76%	6 pts.

Figures compiled by the State Board of Health of Maryland show that, for the past 14 years, 0.17 per cent is the average annual morbidity for typhoid fever. The figures are not available for previous years when the incidence of the disease was higher. The comparison is also not satisfactory because so many of the patients in this study came from other states.

Pregnancy.—Owing to the fact that gall-bladder disease is much more prevalent in women, pregnancy is considered by many as an important etiological factor. There are notes on this condition in 407 of the 496 female patients, and of this number 338 (83%) had had at least one pregnancy before entry (Table IV). Of the 69 females who had not been pregnant, 37 were unmarried, and this brings the percentage of pregnancy among married women up to 91 per cent. Good authorities estimate that 15 per cent of married women of the general population are sterile. Birth statistics for 1919 show that the average number of pregnancies for all ages was 3.4, while the average number of pregnancies per patient in this series is 4.5. Hence it would appear that pregnancy may play some rôle in the incidence of disease of the biliary tract.

TABLE IV.

Relation of pregnancy to case distribution.

Group	No. of females in group	No. of pts. with note	No. who had been pregnant	% who had been pregnant	No. of pts. without note	One pregnancy	2 or 3 pregnancies	4 or 5 pregnancies	5 to 10 pregnancies	Ten pregnancies
Stones in G. B. ..	331	264	223	84	17	10%	28%	22%	33%	7%
Stones in C. D. ..	92	81	67	83	4	8%	25%	19%	43%	5%
Without stones ..	73	62	48	77	3	22%	20%	36%	20%	2%
Total ...	496	407	338	83	24	11%	26%	23%	34%	6%

Other factors often considered as etiological, such as preceding infectious diseases and infections following childbirth, were not tabulated.

Symptoms. Interval between the first symptom and entry into the hospital.—The time interval separating the first symptoms suggestive of disease of the biliary tract

and admission to this hospital varies greatly (Table V). The time as a whole is much shorter for the group without stones, which might mean that the stones did not have time to form in most of these cases. Thirty per cent of the group with stones had had symptoms for more than five years preceding entry, while less than 21 per cent of the group without stones had had symptoms for as long a period. Fifty per cent of the group without stones had had symptoms for less than a year, while 39 per cent in the other two groups had had them for the same length of time.

TABLE V.

Relation of interval between the first symptoms and entry into the hospital to case distribution.

Group	Number of patients	Interval between first symptom and entry into the hospital														
		1 day	5 days	1 mo.	3 mos.	6 mos.	1 year	3 years	5 years	8 years	10 years	15 years	20 years	30 years	40 years	50 years
Stones in G. B...	456	9	13	35	29	42	61	67	72	25	38	28	21	13	2	1
Stones in C. D...	137		1	5	8	10	18	22	23		23	12	9	5		1
Without stones	136	1	5	20	10	11	20	24	17	7	7	7	7			
		%	%	%	%	%	%	%	%	%	%	%	%	%		
Total	729	1	3	8	7	9	14	15	15	5	10	6	5	3		

Initial Symptom.—In 69 per cent of the cases with notes on this point, pain was the first symptom remembered (Table VI). It is natural that it should hold such a prominent place in the history, as it is apt to make a firm impression on the patient. The percentage was lowest in the groups without stones. Indigestion (16%) was the next most common symptom.

TABLE VI.

Relation of initial symptom to case distribution.

Groups	Number of patients with notes in regard to first symptoms	Initial Symptom							
		Pain %	Indigestion %	Nausea or vomiting %	Jaundice %	Chills and fever %	Eructation Gas %	Abdom. soreness %	Malaise and weakness %
Stones in G. B.	455	74	15	3	1	1	1	1	0.3
Stones in C. D.	138	62	23		6	2	2	2	1
Without stones	132	56	15	5	2	3	2	5	3
Total	725	69	16	3	2	1.5	1.5	2	1

In addition to the symptoms listed in Table VI, constipation was the first thing complained of by four patients, a palpable mass by three, itching of the skin by three, diarrhoea by one, loss of weight by one, arthritis by four, flatulence by one, nervousness by one, headache by one, backache by three, dark urine by one, burning in the epigastrium by five and the finding of a stone in the stool by one.

There were intervals of almost entire freedom from untoward symptoms in 82 per cent of the patients with stones in the gall-bladder; in 71 per cent of those having stones in the common duct and in 71 per cent of those without stones.

Individual Symptoms.—In Table VII are tabulated the number of cases in which the various symptoms are described and the percentage of patients who complained of indigestion, nausea, vomiting, constipation, eructation of gas, chills and fever, and loss of weight. Twenty per cent of the patients thought that the taking of food was responsible, in part at least, for bringing on an attack.

TABLE VII.

Relation of various symptoms to case distribution.

Groups	Indigestion		Nausea		Vomiting		Constipation		Eructation of gas		Chills and fever		Loss of weight	
	No. of cases with notes	Present %	No. of cases with notes	Present %	No. of cases with notes	Present %	No. of cases with notes	Present %	No. of cases with notes	Present %	No. of cases with notes	Present %	No. of cases with notes	Present %
Stones in G.B.	454	85	446	77	446	74	405	63	375	58	307	57	287	62
Stones in C. D.	139	93	132	84	132	81	121	71	118	67	106	83	104	82
Without stones	136	82	135	66	135	62	120	52	119	52	100	54	95	60
Total	729	86	713	76	713	73	646	62	612	59	513	62	486	66

Table VII merely shows the high incidence of all of these symptoms in each group. Each of them occurred most frequently in the group with stones in the common duct and least frequently in the group without stones.

Jaundice and itching of the skin.—It is seen from Table VIII that there is a positive history of jaundice more than twice as often in the group with stones in the common duct as in the other two, and that jaundice is almost as common in the group with stones in the gall-bladder. Jaundice was persistent much more frequently in the common-duct group, and itching of the skin was present in this group as compared with the others in the ratio of 9:1.

TABLE VIII.

Jaundice and its character.

Groups	Jaundice		Character of jaundice			Itching of skin	
	No. cases with note	Present per cent	Intermittent %	Constant per cent	Questionable cases	Cases with note	Present per cent
Stones in G. B.....	453	44	92	8	8	343	6
Stones in C. D.....	139	91	58	42		83	52
Without stones	136	37	82	18	1	118	6
Total	728	55	86	14	9	544	13

Pain.—Pain is the most constant symptom recorded. It was present in 96 per cent of all cases, the highest percentage being in the group with stones in the gall-bladder. In 41 per cent of all cases it was described as occupying the entire right upper quadrant; in 29 per cent as being confined to the epigastrium usually toward the right side; and in 13 per cent as being confined mainly to the right hypochondrium. These locations do not include the radiations of pain that will be described later. The groups run fairly parallel as regards the location of the pain, except that it was slightly more diffuse in the group without stones.

TABLE IX.
Pain and its location.

Groups	No. of cases with notes	Present per cent	R. U. Q. per cent	Rt. hypo. per cent	Epigastrium per cent	R. L. Q. per cent	Upper half abd. %	Right half abd. %	Diffuse abd. %	Pelvis per cent	L. L. Q. per cent	Joint per cent
Stones in G. B...	456	98	39	15	29	3	2	6	6	0.2	0.2	0.2
Stones in C. D...	139	95	46	8	34	1	2	4	4	1		
Without stones	136	90	41	10	24	2	2	2	17			2
Total	731	96	41	13	29	2	2	5	8			

Referred Pain.—Radiation of pain was complained of in 51 per cent of the cases (Tables X, XI), the percentage in groups with stones being almost twice as high as in those without stones. In the great majority, the radiation was either to the right shoulder or right back.

TABLE X.
Radiation of pain.

Groups	No. of patients in groups	No. of cases with notes	Per cent with radiation
Stones in G. B.....	460	458	55
Stones in C. D.....	139	136	59
Without stones	136	136	33
Total	735	730	51

TABLE XI.
Location of radiation of pain.

Groups	Rt. shld. per cent	Rt. shld. & back %	Both shlds. Per cent	Rt. shld. Per cent	Rt. back Per cent	Down legs Per cent	Rt. side Per cent	Xiphoid Per cent	Chest per cent	Lt. flank Per cent	Lt. arm Per cent	Lumbar region %
Stones in G. B...	38	11	9	33	2	1	3	1	1	1	0.4	
Stones in C. D...	44	6	6	35			4		2			2
Without stones ...	40	11	7	38	1							2
Total ...	40	10	8	34	1		3		1			1

Character of attacks.—The attacks of pain were considered typical of biliary colic in 81 per cent of the cases in the entire series, the smallest percentage (57) occurring in the group without stones, and the highest percentage (88) in the group with the stones in the common duct.

Physical Examination.—Jaundice was present on admission to the hospital almost three times as frequently in cases of stones in the common duct as in the other groups. The liver was thought to be enlarged in 22 per cent of cases, the highest percentage falling in the group with stones in the common duct. The gall-bladder was palpable in 22 per cent of the cases, and, as would be expected, the highest percentage (over 2:1) falls in the group with stones in the gall-bladder. Tenderness on palpation was present in the right upper quadrant in 77 per cent, and muscle spasm in 44 per cent of the cases, the groups running quite parallel. Acute pain was noted on examination at entry in 31 per cent of patients, the highest number falling in the group with stones in the common duct. The temperature readings are not completely worked out.

TABLE XII.
Findings on physical examination.

Groups	No. of cases in groups	Jaundice		Enlarged liver		Palpable gall-bladder		Tenderness	
		No. cases with note	Positive per cent	Number with note	Enlarged per cent	Number with note	Positive per cent	Number with note	Positive per cent
Stones in G. B....	460	448	30	451	22	443	28	441	78
Stones in C. D....	139	138	80	138	38	134	12	137	72
Without stones	136	136	24	136	6	133	12	135	78
Total	735	724	39	725	22	710	22	713	77

TABLE XII.—(Continued)

Groups	Muscle spasm		Acute pain		Temperature elevation	
	Number with note	Positive per cent	Number with note	Positive per cent	Number with note	Positive per cent
Stones in G. B....	432	44	443	30	275	22
Stones in C. D....	134	43	130	39	69	38
Without stones ..	134	46	129	26	89	23
Total	700	44	702	31	433	25

Laboratory Findings.—The studies on bile in the stool and urine show abnormal findings much more often in the common-duct-stone group than in the other two groups, the ratio on stool examinations being 9:1, and on urine analyses 4:1.

These figures are not wholly reliable. This is shown by a study of the urine analyses in the group with stones in the common duct in which bile was present in only 50 per cent, whereas 86 per cent of these same patients had jaundice on physical examination. All patients with the least jaundice should give a positive test for bile in the urine.

The white blood counts are surprisingly low—only 4 out of 458 being above 25,000. The groups run quite parallel as regards counts.

The gastric analyses are interesting only in the fact that there was no free HCl in 23 per cent of 206 analyses. The highest percentage with this absence was in the group with stones in the common duct. It is maintained by some that achlorhydria results from removal of the gall-bladder.

X-ray reports as regards stones are recorded in only 99 cases—in 13 per cent positive. Of those taken in the common-duct group 19 per cent, and of those with stones in the gall-bladder 11 per cent were positive.

TABLE XIII.
Laboratory findings.

Groups	No. of cases in groups	Stool examination		Urine examination	
		No. with note	Per cent abnormal	No. with note	Per cent abnormal
Stones in G. B..	460	296	4	405	14
Stones in C. D..	139	79	26	116	50
Without stones .	136	99	2	123	9
Total	735	474	7	744	17

TABLE XIII.—(Continued)

Groups	White blood counts						Free HCl			
	Number with note	Below 11,000 %	11,000 to 16,000 %	16,000 to 25,000 %	Above 25,000 %	Highest W. B. C.	Number with note	No free HCl %	Normal per cent	High per cent
Stones in G. B..	271	70	20	9	1	48,000	123	24	72	3
Stones in C. D..	90	72	17	11	1	27,000	33	33	58	9
Without stones.	97	72	16	12			50	14	86	
Total	458	71	19	10	1		206	23	73	4

OPERATIONS

Operators and Mortality.—As stated before, there are 735 cases in the three groups. Of these operations, 720 were performed by 18 different surgeons, each of them doing at least five of the operations. The mortality percentage varied from nil to 19 per cent. The other fifteen operations were performed by seven different surgeons, the mortality being 27 per cent.

Table XIV refers to operators who performed five or more operations. When more than one operation was performed on a patient, the operator performing the first one is credited with the case unless the subsequent operation was fatal. It is quite striking that the mortality percentage is much lower now than it was in the first days of the hospital. The last four residents in surgery have performed a total of 153 of these operations with only two deaths—a mortality of 1.3 per cent. One performed 65 operations without a single death.

TABLE XIV.
Operators and mortality percentages.

Operator	Stones in G. B.			Stones in C. D.			Without stones			Total		
	No. of cases	No. of deaths	Mortality per cent	No. of cases	No. of deaths	Mortality per cent	No. of cases	No. of deaths	Mortality per cent	No. of cases	No. of deaths	Mortality per cent
No. 1..	120	8	7	41	9	22	37	1	3	198	18	9
No. 2..	66	7	11	37	9	24	9	1	11	112	17	15
No. 3..	44	2	5	12	2	17	21	1	5	77	5	7
No. 4..	32	0	0	9	0	0	14	0	0	65	0	0
No. 5..	31	1	3	1	0	0	8	0	0	40	1	2.5
No. 6..	29	0	0	6	0	0	2	1	50	37	1	2.7
No. 7..	14	0	0	7	4	57	5	0	0	26	4	15
No. 8..	11	0	0	5	3	60	9	0	0	25	3	12
No. 9..	20	1	5	2	2	100	3	0	0	25	3	12
No. 10..	17	1	6	5	2	40	2	0	0	25	3	12
No. 11..	16	2	13	2	0	0	6	2	33	24	4	17
No. 12..	11	1	9	0	0	0	6	0	0	17	1	6
No. 13..	13	1	8	1	1	100	2	1	50	16	3	19
No. 14..	3	0	0	6	0	0	3	2	67	12	2	17
No. 15..	6	0	0	2	0	0	3	0	0	11	0	0
No. 16..	7	0	0	0	0	0	2	0	0	9	0	0
No. 17..	5	1	20	0	0	0	2	0	0	7	1	14
No. 18..	4	0	0	1	0	0	0	0	0	5	0	0

Operative approach.—A right rectus incision was employed at the first operation in all except three cases.

Free peritoneal fluid was present in 45 cases (6%), and localized abscesses in nine cases. This fluid was described as being straw-colored in 24 cases, as bile-stained in 16 cases, as unmistakable pus in 4 cases and in one as much fibrin with little fluid.

Adhesions in the right upper quadrant were noted and described in 73 per cent of 727 cases. In 42 per cent they were rather numerous, while in 31 per cent they were few in number. The only interesting comparison between the groups lies in the higher percentage of adhesions and their greater density in the group with stones in the common duct.

TABLE XV.
Free peritoneal fluid and nature of adhesions.

Groups	Number in group	Free peritoneal fluid		Adhesions			
		No. cases with notes	Present per cent	No. cases with notes	Many adhesions per cent	Few adhesions per cent	No adhesions per cent
Stones in G. B.	460	460	7	455	37	29	34
Stones in C. D.	139	139	3	137	61	30	9
Without stones	136	136	7	135	38	38	24
Total	735	735	6	727	31	31	27

Liver and Gall-bladder.—The liver was enlarged in 19 per cent of the cases. The highest percentage is in the common-duct group. On physical examination, the liver was thought to be enlarged in 22 per cent of the cases.

The gall-bladders were described in various terms in the operative notes (Table XVI). The main points of interest in comparing the groups are: (1) The high percentage of distended gall-bladders in the stones in the gall-bladder or cystic duct group, the ratio being more than 2:1 as compared with that in the other groups. (2) The high percentage of gall-bladders normal in size but having thick walls in the group without stones. (3) The high percentage of small and contracted gall-bladders in the group with stones in the common duct.

TABLE XVI.

Description of gall-bladders (macroscopically).

Groups	No. cases described	Description of gall-bladder						
		Enlarged per cent	Large and distended per cent	Thick wall, normal size per cent	Small and contracted per cent	Perforated per cent	Dense adhesions per cent	Normal per cent
Stones in G. B...	459	13	64	12	11	1		12
Stones in C. D...	137	28	22	11	36	1	4	26
Without stones..	135	14	30	28	4			38
Total	731	19	50	15	14	1	1	20

Position of Stones.—In the group with stones in the gall-bladder or cystic duct they were found in the cystic duct in 43% of the cases, and in the cystic duct alone in 27 (6%) of the cases. In the second group stones were present in the common duct in all except three cases and these patients had stones in the hepatic duct. In addition 15 patients had material described as sand or mud in the common duct.

TABLE XVII.

Position of stones.

Groups	Number of cases	Stones in G. B.		Stones in cyst. duct.		Stones in C. D.		Stones in hep. duct.	
		No. cases with note	Present per cent	No. cases with note	Present per cent	No. cases with note	Present per cent	No. cases	Present per cent
Stones in G. B...	460	460	94	460	43	460	0	460	0
Stones in C. D...	139	136	58	139	15	139	98	139	5
Total	599	596	86	599	36	599	23	599	1

In addition to the figures given in the chart, other stones in the "stones in the gall-bladder group" include those free in the peritoneal cavity in one per cent, in a diverticulum of the gall-bladder in 0.2 per cent, in adhesions around the gall-bladder in one per cent, in abscess pouches in one per cent and in the liver substance in 0.2 per cent of the cases.

Macroscopic study of fluid contents of the tract.—In 47 per cent of the cases, this fluid was abnormal in appearance; in some cases this merely means that the bile was thick and tenacious. Cultures taken at the operation were positive in 58 per cent of the cases. The operative notes stated that there was an empyema of the gall-bladder in 17 per cent and a hydrops in 9 per cent of the cases. The highest percentage of abnormal contents is found in the group with stones in the gall-bladder.

TABLE XVIII.

Character of fluid in the biliary tract.

Group	Number of cases	Number of cases with notes	Character of fluid in biliary tract						
			Normal per cent	Thickened, tenacious %	Definite pus per cent	Mucus per cent	Mucopurulent %	No fluid per cent	Bile and mucus %
Stones in G. B.....	460	409	49	12	18	12	8	1	
Stones in C. D.....	139	112	63	25	8	2			2
Without stones	136	128	58	26	15	2			
Total	735	649	53	17	15	8			

Treatment of the gall-bladder and ducts at operation.—In the first group with stones in the gall-bladder and cystic duct, the gall-bladder was removed in 244 cases, partially removed in three cases, drained in 211 cases, opened and closed tightly in one case, and in one case a gastroenterostomy was performed without further operation. In the cases drained without cholecystectomy, a tube was placed in the gall-bladder in 196 cases, and drains were placed down to the gall-bladder without a tube in 11 cases. The common duct was opened in 32 of the 460 cases; in 4 of these accidentally and in the remainder during the search for stones. In only 7 cases of this group was the abdomen closed tightly without drainage. Considering the 244 cases in which a cholecystectomy was performed, we find that the cystic artery was ligated with silk in 136 cases, with catgut in 59, with silk and catgut in six, the material used not being stated in 43 cases. The cystic duct was ligated with silk in 102, with catgut in 56, with silk and catgut in 40 cases. A tube was placed in the cystic duct stump in 23 cases and drains alone placed down to the stump in three cases (the material used not being stated in 20 cases). In the 32 cases in which it was opened, a drainage tube was placed in the opening in the common duct in 9 cases, in the cystic duct in 12 cases; and in the remainder the common duct was closed tightly.

Passing to the second group (with stones in the common duct) we find that the common duct was opened in 127 of 138 cases. In 49 per cent of these a tube was sewed into the common duct, usually with catgut. The common duct was closed with silk in 17 cases, with catgut in 24 cases, with silk and catgut in 7 cases, the material used not being stated in 17 cases. A tube was placed in the cystic duct in 24 of the cases in which the common duct was closed. Drains were placed in the proximity of the duct in most of the others. One case was closed tightly and in three cases stones were removed by the transduodenal route. The duodenum was probed through the common duct at the time of the operation in all but 15 cases. This was found to be impossible in some instances and in others no effort was made. It is significant that in 7 of these 15 cases subsequent operations had to be performed for stones in the common duct.

Studying next the group without stones, one finds that in 57 cases a cholecystectomy was performed; in 2, partial removal; in 74, a cholecystostomy; in one, a choledochotomy; and in 2, a choledochostomy. In the cases with removal of the gall-bladder, the cystic artery was ligated with silk in 35; with catgut in 14; with silk and catgut in 2; the material used not being stated in 6 cases. The cystic duct was ligated with silk in 23 cases, with catgut in 9, with silk and catgut in 16, the material used not being stated in 5 cases; and a tube was placed in the cystic duct in 4 cases. The abdomen was closed tightly without drainage in 3 cases in this group. The common duct was opened in 3 cases; in one case it was closed tightly and in 2 cases a tube was placed in it.

TABLE XIX.
Types of operations.

Group	No. of cases	Cholecyst-ectomy	Partial cholecyst-ectomy	Drainage	Choledo-chotomy	Choledo-chostomy
Stones in G. B...	460	244	3	211		
Stones in C. D...	139	65		45		62
Without stones ...	136	57	2	74	1	2

TABLE XX.
Treatment of cystic artery and duct.

Group	Cystic artery ligated with				Cystic duct treated with					
	Silk	Catgut	Both	Material, no note	Silk	Catgut	Both	Tube in	Drain to	Material, no note
Stones in G. B..	136	59	6	43	102	56	40	23	3	20
Stones in C. D..	18	5		42	6	7	6	24		22
Without stones .	35	14	2	6	23	9	16	4		5

Other pathological conditions in the abdomen.—Of the patients operated upon, 25 per cent showed definite pathological conditions in addition to those affecting the biliary tract.

The pancreas was indurated in 36 of the 735 cases. In 20 of these cases this condition was associated with stones in the gall-bladder; in 9 with stones in the common duct and in 7 of the group without stones.

The appendix was removed at the time of the gall-bladder operation in 129 cases, and in 109 of these it was found to be diseased, in 70 cases in the group with stones in the gall-bladder, in 2 with stones in the common duct and in 37 in the group without stones. It is interesting that the number in the group without stones is so large. The appendix had been removed at a previous operation in 38 cases.

Other pathological lesions found were: carcinoma of the pancreas (2 cases); ventral hernia (1 case); myomata uteri (2 cases); enlarged spleen (2 cases); carcinoma of the stomach (4 cases); gastric ulcer (5 cases); duodenal ulcer (3 cases); fat necrosis (3 cases); hypernephroma (1 case); diverticulum of the cystic duct (2 cases); other local abscesses (4 cases); general peritonitis (1 case); kidney stones (1 case); typhoid enteritis (1 case); diverticulum of the stomach (1 case).

Enlarged glands along the ducts were described in 11 of the cases with stones in the gall-bladder, in 3 of the cases with stones in the common duct, and in 5 of the cases in the group without stones.

Anatomical peculiarities are not described in much detail in the operative notes. These pecularities include (1) four cases with a very short cystic duct; (2) one case with the cystic duct entering the common duct from behind; (3) two with the cystic duct running parallel to the common duct; (4) three with quite dense strictures of the cystic duct, although there had been no previous operation; (5) one with all the ducts of enormous size, greatly dilated; (8) two with a very long hepatic artery and (9) one with an aberrant pancreas.

Remarks.—The clinical pre-operative diagnosis was essentially correct in all cases except two in the group with stones in the gall-bladder, one in the group with stones in the common duct and fifteen in the group without stones.

The prognosis at the completion of the operation was considered very poor in 21 cases in the first group; in 13 in the second and in 9 cases in the group without stones.

Bacteriological Studies.—Reports on the cultures taken at the time of operation are found in only 270 cases. The cultures were taken from the fluid contents of the biliary tract in nearly every case. Of these, 58 per cent were positive, the highest percentage being in the group with stones in the common duct and the lowest in that group without stones. This is in harmony with the belief that infection plays an important part in the formation of stones. *B. coli* was the predominating organism with 49 per cent and *B. typhosus* next with 19 per cent.

TABLE XXI.
Bacteriological studies.

Groups	Number of cases	Number of reports	Positive per cent	Number of cases giving positive cultures and organisms							
				B. coli per cent	B. typhosus per cent	Staph. aureus per cent	Staph. albus per cent	Strept. non-hemolyticus %	B. coli and Strept. %	B. coli and Staph. %	B. lactis aerogenes %
Stones in G. B. ...	460	170	61	45	21	8	9	5	3	1	3
Stones in C. D. ...	139	50	74	27	4	1			2	1	1
Without stones	136	50	33	5	5	1	1		1	1	
Total	735	270	58	49	19	6	6	3	4	2	3

The positive cultures, in addition to those given in Table XXI, were streptococcus viridans (1 case), streptococcus hemolyticus (2 cases); B. fecalis alkaligenes and B.

proteus; (1 case each); pneumococcus (2 cases); B. subtilis and diptheroid (1 case each); positive cultures in which there was some doubt as to the organism (4 cases).

Microscopic Pathology.—The gall-bladders were removed in 366 cases and the notes on the microscopic study of 354 of these are tabulated below. The walls were thickened in 93 per cent. Round mononuclear cells were present in all but 6 cases and these were in the group without stones. The mucosa was described as abnormal in 82 per cent of cases. Only three gall-bladders removed were diagnosed as being normal and these were in the group without stones.

TABLE XXII.

Microscopic studies on gall-bladders.

Group	Cholecystectomies	Not studied cases	Thickness of wall		Round cells	
			Thick per cent	Normal per cent	Present per cent	Absent per cent
Stones in G. B.	244	8	224	12	236	0
Stones in C. D.	65	0	65	0	65	0
Without stones	40	4	40	13	47	6
Total	366	12	93	7	98	2

TABLE XXII.—(Continued)

Group	Mucosa					Pathological diagnosis			
	Partly gone %	All gone per cent	Inflam. per cent	Hypertrophy %	Normal per cent	Acute per cent	Sub-acute per cent	Chronic per cent	Normal per cent
Stones in G. B.	103	53	38		37	32	4	200	
Stones in C. D.	14	22	12	7	10	4	1	60	
Without stones	13	10	3	7	20	4	3	43	3
Total	36	24	15	4	18	11	3	85	1

Number of stones found at operation.—There are estimates as to the number of stones found at operation in 582 cases with stones. In 18 per cent, only one stone was found; in 43 per cent, between 1 and 10 stones and in 39 per cent more than 10 stones were found. The two groups with stones run parallel as to their number. The types of stones are described in too few cases to warrant tabulation.

Post-operative notes.—In the group with stones in the common duct, the last drain was removed in less than 5 days in 18 cases, between 5 and 10 days in 43 cases, between 10 and 20 days in 7 cases, (no note in 34 cases, and 33 cases not included because of death). The drainage tube was removed in less than 5 days in 8 cases, between 5 and 10 days in 37 cases, between 10 and 20 days in 16 cases, (no tube placed in 16 cases, no note in 29 cases and death in 33 cases).

Considering the other two groups, we find the date of removal of the drainage tube is noted in 194 cases—within less than 5 days after operation in 11 per cent, between 5 and 10 days in 54 per cent, between 10 and 20 days in 34 per cent, and after 20 days in 2 per cent.

Table XXIII showing how long post-operative drains were left in, in the group with stones in the gall-bladder and in the group without stones, is divided into (1) Cholecystectomy, (2) Drainage of Gall-bladder. It is quite apparent that the last drains were removed much sooner in the cases of resection of the gall-bladder.

TABLE XXIII.

Time of removal of last drain.

Groups	No. cases in group		Less than five days		Five to ten days		Ten to twenty days		Cases without notes and mortalities	
	Cholecystectomy	Drainage	Cholecystectomy per cent	Drainage per cent	Cholecystectomy per cent	Drainage per cent	Cholecystectomy per cent	Drainage per cent	Cholecystectomy cases	Drainage cases
Stones in G. B.	244	211	72	24	83	88	14	30	75	69
Without stones	57	74	17	4	16	30	1	10	21	29
Total	301	285	43	15	48	63	8	22	96	98

The time at which the drainage of bile ceased and the condition of the incision on discharge from the hospital will now be considered. Owing to the variety of operations, the cases with stones in the common duct are not included in Table XXIV. In 4 cases in this group there was no drainage of bile after operation; in 10 the drainage stopped between 5 and 10 days; in 35 cases between 10 and 20 days; in 31 cases between 20 and 40 days; in 14 cases bile was still being discharged when the patient left the hospital; in 12 cases the notes do not give the date at which the drainage ceased, and the 33 deaths are not included. If we exclude patients who died while in the hospital and those others about whom there is no definite note, we find that the incision was completely healed on discharge from the hospital in 60 per cent of cases; that there was a very superficial unhealed area in 13 per cent; and that there was a deep sinus in 27 per cent. In one-half of the cases with a deep sinus bile was still being discharged.

In Table XXIV the group with stones in the gall-bladder and the group without stones are considered. The percentages listed on the line headed "Total" do not include the patients dying shortly after operation and the cases in which there was no definite note.

They show that 93 per cent of the drained gall-bladders were discharging bile for more than 10 days after operation, while in only 38 per cent of the cholecystectomies was there any post-operative draining of the bile. More than four times as many of the drained gall-bladders were still discharging bile through the incision when the patients left the hospital. Those figures at least demonstrate the immediate advantage of resection over drainage. The patients in the former group are in the hospital for a shorter period of time and are in better condition on discharge from the hospital.

TABLE XXIV.

Drainage of bile after operation.

Groups	No. of cases in groups		No drainage after operation		Less than five days		Five to ten days		Ten to twenty days		Twenty to forty days		Draining on discharge		Time doubtful		Dead	
	Excision	Drainage	Excision per cent	Drainage per cent	Excision per cent	Drainage per cent	Excision per cent	Drainage per cent	Excision per cent	Drainage per cent	Excision per cent	Drainage per cent	Excision per cent	Drainage per cent	Excision cases	Drainage cases	Excision cases	Drainage cases
Stones in G. B.....	244	211	137	2	8	0	17	8	37	63	11	60	18	55	3	10	13	13
Without stones	57	74	36	2	0	0	6	4	1	21	9	18	1	16	3	8	1	5
Total	301	285	62	1.5	3	0	8	8	13	34	7	31	7	29	6	18	14	18

TABLE XXV.

Condition of incision on discharge.

Groups	Completely healed		Almost healed		Deep sinus		No note	
	Excision per cent	Drainage per cent	Excision per cent	Drainage per cent	Excision per cent	Drainage per cent	Excision cases	Drainage cases
Stones in G. B....	181	113	24	17	22	55	4	13
Without stones ..	48	40	7	7	1	21		1
Total	81	60	11	10	8	29	4	14

Data on the bile contents of the stool and urine at time of discharge from the hospital and also the time of disappearance of bile from the urine and its presence in the stool were too meagre to be of any real value.

Length of stay in hospital.—Table XXVI shows the length of stay in hospital of these patients except those who died shortly after operation. The time is relatively longer for the common duct stone cases than for others. The average stay in the hospital of all patients on all services excepting psychiatry is 18 days.

TABLE XXVI.

Length of stay in hospital.

Time in days	Stones in G. B.	Stones in C. D.	Without stones	Per cent
10 to 20.....	70	10	16	14
20 to 30.....	191	38	47	42
30 to 40.....	107	28	36	26
40 to 50.....	42	13	15	11
Longer	22	17	13	8
Total	432	106	127	

Cases in which one or more additional operations became necessary.—There are 80 patients (11 per cent) of 735 in the three groups who required more than one operation on the biliary tract. Of these 38 were in the group with stones in the gall-bladder, 34 with stones in the common duct and 8 in the group without stones. These figures do not include patients who might have been operated upon at other hospitals since their last visit here, as the records would be incomplete. Nor does it include 3 patients submitted to a second operation for drainage of hepatic abscesses, one having a second operation for acute pancreatitis, and another case in which adhesions were released at the second operation.

Of the 80 patients, 42 had the first operation performed at another hospital and a second operation here, while 38 had two or more operations here. Of the patients with stones in the common duct, two had 4 operations each and 5 had 3 each. Of the 80 patients only 9 (11 per cent) had had the gall-bladder removed, while 71 (89 per cent) had had the gall-bladder drained at the original operation. Of the 9 patients operated upon a second time following cholecystectomy seven had stones in the common duct, the other two had stones in the gall-bladder and underwent a plastic operation for stricture of the common duct caused by injury incurred during the cholecystectomy.

In one patient requiring re-operation for stones only the common duct was opened at the original operation and in another case a second operation was performed for excision of a fistulous tract.

The time elapsing between operations varied between 4 days and 15 years. In 15 cases the second operation followed the first in less than 3 months, in 13 cases after from 3 to 6 months, in 17 cases after from 6 months to 1 year, in 11 cases after from 1 to 3 years, in 13 cases between 3 and 5 years, in 7 cases between 5 and 10 years and in 4 cases between 10 and 15 years. Thus we see that, of these patients needing re-operation, in 56 per cent it became necessary in less than 1 year and in 86 per cent in less than 5 years. When more than two operations were performed, the shortest interval separating them has been taken. The groups run quite parallel as regards the interval between operations.

As regards the location of the stones, there were 3 cases in the group with stones in the gall-bladder in which no stones were found at the first operation but were found at the second operation and in 7 cases stones were found at the first operation and not at the second. Of the 38 patients in this group fourteen had a persistent fistula between operations.

At the original operation in the group with stones in the common duct the stones found were in the gall-bladder or the cystic duct alone in 17 cases (50 per cent), in the common duct alone in 3 cases (9 per cent), in both common duct and gall-bladder in 4 cases (12 per cent). No stones were found in 6 cases (19 per cent) and the location is not known in 3 cases (10 per cent). Stones

were found in the common duct in only 7 cases (21 per cent). The patient's word for the location of stones at previous operations had to be taken in quite a few cases.

A study of the condition since the last operation in 38 patients re-operated upon with stones in the gall-bladder showed that 22 were well (at least up to the time of death from some other trouble), 5 patients were improved; we had no reply in 5 cases, and 7 patients were dead. No reply was received from two of the patients operated upon more than once in the common duct group; nineteen of the patients were well and thirteen were dead. Five of the patients in the group without stones who had been operated upon more than once were well when last heard from; one was improved, one was unimproved and no reply was received in 2 cases.

Ultimate results.- The cases are divided into 7 groups; (1) Patients dying after operation during the same admission to the hospital, (2) Patients well at the last reply. If they had been entirely free from gall-bladder symptoms for at least one year and then died of some other disease they were considered as cured. (3) Patients definitely improved by operation but not entirely well, (4) Patients not improved by operation or who had a recurrence of symptoms later. In the 80 cases in which there was more than one operation the last is the one considered. (5) Patients dying in less than one year after discharge from the hospital of some sickness other than gall-bladder disease. These are not listed as cures or fatalities. (6) Patients who died more than one year after leaving the hospital in whom the cause of death was not known but was thought not to be a recurrence of their former trouble. (7) Cases not followed.

The number of cases in each group are given in Table XXVII, eighty-two per cent of the patients have been followed.

TABLE XXVII.

Ultimate results according to arbitrary divisions.

Groups	No. of cases	Class I	Class II	Class III	Class IV	Class V	Class VI	Class VII
Stones in G. B....	460	28	263	40	21	11	7	90
Stones in C. D....	139	33	83	6	5		2	10
Without stones ..	136	9	68	17	7	2		33
		%	%	%	%	%	%	%
Total	735	9.5	56	8.5	4.5	2	1	18

The cases in the seven classes will be considered in the order named. *Class I.*—Of the 735 patients operated upon, 9.5 per cent died while in the hospital, the mortality being highest among those with stones in the common duct—24 per cent for this group. Of the 70 patients in this class, in 33 the gall-bladder was drained, in 27 it was removed, in 7 a choledochostomy was performed; two were submitted to an exploratory laparotomy and one to a choledochotomy.

The causes of death were: (1) Twenty-one patients (30 per cent) died of peritonitis. The gall-bladder was drained in 12 of these; in 7 it was excised; in 2 the common duct was drained. In one case the wound was closed without drainage. The average time that these patients lived was 8 days. (2) Eight patients (11 per cent) died as a result of hemorrhage. Of these two had had the gall-bladder removed, in two it had been drained, in one a choledochotomy, in one a choledochostomy, in one an exploratory laparotomy had been done. The average time between operation and death was 5 days. (3) Eight patients (11 per cent) died of pneumonia, after an average lapse of 14 days. (4) Four died from pulmonary embolism (in three the gall-bladder had been drained and in one it had been excised). The average time before death was 8 days. (5) Eight died from weakness and shock in an average of 4 days after operation. In four a cholecystectomy was performed and in four a cholecystostomy. One of these patients died on the table, but in addition to his biliary tract disease he had a pancreatitis and fat necrosis. (6) Four patients died because of persistent drainage of bile and continued fever. (7) In the remaining cases, the causes of deaths were: nephritis (2), abscesses (2), leukemia (1), pancreatitis (1), intestinal obstruction (1), typhoid fever (1), cholangitis (1), hematemesis (1), infected incision in a demented patient (1), oedema of lungs (1), carcinoma of the pancreas (1), obstruction from remaining stones (3). In one case the cause of death was not ascertained.

Of the 70 patients, 27 had definite pathological conditions in addition to those present in the biliary tract. These consisted in: diabetes (1 case); retroperitoneal abscesses (2 cases); lung abscess (1 case); liver abscesses (4 cases); other extra-gall-bladder abscesses (2 cases); cirrhotic liver (1 case); typhoid enteritis with positive blood cultures (2 cases); ascites and anemia (1 case); a large carcinomatous mass in the right upper quadrant (1 case); gall-bladder-duodenal fistula (1 case); general peritonitis not caused by biliary tract trouble (2 cases); carcinoma of the pancreas (2 cases); pancreatitis (4 cases); leukemia (1 case); duodenal ulcers (2 cases).

The above probably played a large part in causing deaths, as many patients who would just have been able to survive a severe operation were overcome by the additional load.

In an attempt to find some points which would give some lead as to prognosis, the cases of the patients dying in the hospital are analyzed in detail. The 33 cases of stone in the common duct are given in Table XXVIII.

TABLE XXVIII.

Analysis of deaths in group with stones in the common duct.

Case No.	Cause of death	Days lived	Time since typhoid	Duration symptoms	Jaundice character	Previous operations	Adhesions	Position of stones	Operation	Other pathological conditions
1	Peritonitis	10	No T.	7 yrs.	Intermit.	Drainage of G.B. 4 yrs. before	Many	Ampulla	Transduodenal removal stones	None
2	Peritonitis, Fecal fistula	8	23 yrs.	4 yrs.	Constant	Cholecystect. 9 days before	Many	Ampulla	Transduodenal Removal	None
3	Peritonitis	7	30 yrs.	2 yrs.	Constant	None	Many	C. D.	Cholecystostomy Choledochotomy	None
4	Hemorrhage Peritonitis	12	5 yrs.	5 yrs.	Constant	Cholecystos. 1 yr. before	Many	Hep. Duct	Choledochostomy	None
5	Fecal fistula Pneumonia	14	No T.	3 yrs.	None	None	Few	C. D.	Choledochostomy	None
6	Hemorrhage Pneumonia	6	No T.	8 yrs.	Intermit.	None	Many	G. B. & C. D.	Cholecystectomy Choledochostomy	Duodenal ulcer
7	Pneumonia. Portal thrombosis	5	20 yrs.	7 yrs.	Constant	None	Few	G. B. & C. D.	Cholecystectomy Choledochostomy	None
8	Nephritis	3	No T.	7 yrs.	Intermit.	Cholecystec. 9 yrs. before	Many	Ampulla	Choledochostomy	Pancreatis
9	Suppression of Secretions	1	2 yrs.	2 yrs.	Constant	Cholecystos. 9 mos. before	Many	Ampulla	Choledochostomy	None
10	Leukemia	30	6 yrs.	5 yrs.	Intermit.	Cholecystec. 3 yrs. before Choledochos. 2 yrs. before	Many	None	Release adhesions	Splenomegaly Leukemia
11	Peritonitis Stone in C. D.	2	20 yrs.	30 yrs.	Intermit.	Cholecystos. 2 yrs. before	Many	C. D.	Cholecystostomy	None
12	Pyrexia Drainage of bile	7	No T.	1 yr.	Intermit.	None	Many	C. D.	Choledochotomy	None
13	Hemorrhage	2	No T.	5 mos.	Intermit.	None	Many	C. and Hep. Duct	Cholecystectomy Choledochotomy	None
14	?	4	No T.	3 yrs.	Yes (?)	None	Many	Ampulla	Cholecystostomy Choledochotomy	None
15	Pneumonia	3	35 yrs.	6 mos.	Constant	None	Many	G. B. & C. D.	Cholecystostomy Choledochostomy	None
16	Peritonitis	5	No T.	12 yrs.	Intermit.	1. Drained 2. Resection 2 yrs. before	Many	Hep. D.	Choledochostomy	None
17	Pneumonia Diabetes	7	?	9 yrs.	Intermit.	Cholecystect. 3 yrs. before Choledochos.	Many	C. D.	Cystice-choledochostomy	Diabetes
18	Peritonitis	3	No T.	1 yr.	None	None	Many	G. B., Hep. and C. D.	Cholecystectomy Cystice-choledochostomy	Local abscess
19	Progressive weakness	12	20 yrs.	5 yrs.	Constant	None	None	Ampulla and C. D.	Cholecystostomy Transduodenal Removal	None
20	Peritonitis	16	No T.	6 mos.	Constant	None	None	C. D.	Choledochostomy	Pancreatiti
21	Shock Pancreatitis	Table	22 yrs.	4 yrs.	Constant	Drained three times	Many	C. D.	Choledochostomy	None
22	Lung abscess	30	No T.	20 yrs.	Intermit.	None	Many	C, D.	Cholecystostomy Choledochotomy	Lung abscess
23	Shock	1	No T.	4 mos.	Constant	None	Many	G. B. & C. D.	Cholecystostomy Choledochotomy	None
24	Hemorrhage	1	No T.	4 yrs.	Constant	None	Many	G. B. & C. D.	Cholecystostomy	None
25	Pyrexia Infection	6	No T.	2 yrs.	Constant	None	Many	G. B., Cyst. and C. D.	Cholecystostomy	Liver abscess
26	Stone in V. A. Obstruction	5	No T.	5 mos.	None	None	Many	G. B., Cyst. and C. D.	Cholecystostomy Choledochotomy	None
27	Pancreatitis	47	?	18 mos.	Intermit.	None	Few	C. D.	Cholecystostomy Choledochotomy	Pancreatitis
28	Pyrexia Vomiting	24	No T.	17 mos.	Intermit.	None	None	C. D.	Cholecystectomy Choledochostomy	None
29	Anuria	12	No T.	7 mos.	Constant	None	Many	G. B., Cyst. and C. D.	Cholecystostomy	Cirrhotic liver
30	Fec. fistula	7	No T.	2 yrs.	Intermit.	Cholecystos., choledochos., 5 yrs. before	Many	C. D.	Cholecystectomy Choledochotomy	None Stricture cystic duct
31	Intest. obstruc. Stone in V. A.	1	?	2 yrs.	None	None	Few	Ampulla	Exploratory laparotomy	None
32	Hemorrhage Stone in C. D.	1	No T.	6 mos.	Constant	None	Few	C. D.	Exploratory laparotomy	Abscess
33	Hemorrhages	Not described in detail				None				
	Total		35%		81%	33%	Dense in 75%			34%

A summary of the table just given shows that 35 per cent had had typhoid fever, a figure which is 7 per cent higher than that for the whole group. The interval between the attack of typhoid fever and admission to the hospital does not seem to have any bearing on the prognosis, nor does the time elapsing between the first symptom and entry seem to be of any significance. The presence of jaundice on physical examination and the white blood counts correspond closely with those for the entire group. Of these patients, 33 per cent had more than one operation, which is 8 per cent higher than for the entire group with stones in the common duct. Two of these patients had had three operations and one had had four. Six of these 11 patients had had the gall-bladder drained at the original operation, in four it had been excised, and in one it had first been drained and later removed. In one of these cases requiring re-operation after a cholecystectomy, the interval between operations was only 9 days, and a stone in the common duct was found to have been overlooked at the first operation. Previous operations evidently make for a worse prognosis. There were very dense adhesions in 75 per cent of the cases. The only thing of interest about the location of the stones in this group is the high mortality associated with those present in the ampulla of Vater.

The fluid contents of the biliary tract were distinctly abnormal in 65 per cent of the fatal cases in which it was described, the percentage for the whole group being only 37. A point of special interest is that 66 per cent of the deaths in this group occurred during an attack at the time of operation, as evidenced by severe pain or fever. This percentage is almost twice as high as that for the whole series. The main point of interest in the operation itself seems to be the high mortality in cases in which stones were removed by the transduodenal route. Thirty-four per cent of these patients had additional pathological conditions.

The 28 deaths in the group with stones in the gall-bladder and the 9 deaths in the group without stones will be considered together. We find that (1) eleven per cent of the patients were more than 60 years of age; (2) nineteen per cent had had typhoid fever; (3) fifty-one per cent had jaundice on entry (this is 23 per cent higher than that when all cases are considered); (4) sixty per cent were in an acute attack as evidenced by acute pain or fever—(this is twice as high as that for all cases in the two groups); (5) the white blood count was above 11,000 in only 4 per cent of cases; (6) fourteen per cent had had a previous operation on the tract—(this is almost twice as high as that for all cases); (7) fourteen per cent had free abdominal fluid; (8) twenty-seven per cent had other abdominal pathological conditions.

In 54 per cent of the last described fatal cases the gall-bladder was drained, in 40 per cent removed, in 3 per cent an exploratory laparotomy, and in 3 per cent a choledochotomy was performed.

It was stated before that only 33 per cent of the patients in these three groups were males, but that these contributed 56 per cent of the fatalities is of interest. Eighty-six per cent of the deaths followed operation by less than 15 days.

Class II. Cures.—This comprises 416 cases, including those patients who were well at the last reply and those who died of some other trouble more than one year after leaving the hospital. The whole number represents 57 per cent of all the cases in the three groups, and 72 per cent of the patients from whom a reply as to their exact condition was obtained.

The cases in the group with stones in the gall-bladder and those in the group without stones will be considered first. There are 263 cases in the former and 68 in the latter. If we consider the cases with partial removal of the gall-bladder as having been drained, we have 173 cases with removal of the gall-bladder, and 158 with drainage.

In addition there is one patient in whose case the gall-bladder was opened and closed tightly, and who is well after 10 years; and another upon whom a choledochostomy and cholecystotomy were performed and who is well after 15 years. As 301 patients in the 2 groups had the gall-bladder removed and 292 had it drained, there is a higher percentage (by 3 per cent) of cures after cholecystectomy. These figures include the patients from whom no reply was received. The following table shows the interval elapsing between operation and the last reply from patients in these two groups, and the operation performed.

TABLE XXIX.

Patients well since operation. Types of operations.

Interval between operation and last reply	Stones in the gall-bladder group		No stones group	
	Cholecystectomy	Drainage	Cholecystectomy	Drainage
3 months	2			
6 months	14	1		
1 year	17	3	4	2
3 years	24	10	14	4
5 years	35	15	3	3
8 years	14	1	2	4
10 years	17	27	4	10
15 years	4	38	1	10
20 years	13	16	3	3
25 years	2	11		
Total	142	122	31	36

Because of the fact that such varied operations were performed on the patients in *the common duct group,* the cases are not listed in a table. Eighty-three patients are considered as cured, this number including 12 patients who died more than 4 years after operation of some other trouble without further disease of the biliary tract.

Forty-six of these patients had a cholecystectomy, one had a partial cholecystectomy, 28 had a cholecystostomy, seven had a choledochostomy without opening of the gall-bladder, and one had the abdomen closed tightly after opening and closure of the gall-bladder. The common duct was opened in almost every case, and closed in about half of them. The interval separating the operation and last reply was less than 3 years in 10 cases, between 3 and 5 years in 12 cases, between 5 and 10 years in 17 cases, between 10 and 20 years in 27 cases, and between 20 and 30 years in 17 cases.

Among these 416 patients listed as cured are 48 who died more than one year after leaving the hospital of some other trouble. Of these, 23 are in the group with stones in the gall-bladder, 12 in the group with stones in the common duct and 13 in the group without stones. The causes of death were accidents (3); cardiac disease (6); pulmonary tuberculosis (5); tuberculous meningitis (1); tuberculous peritonitis (1); carcinoma of rectum (1); cerebral accident (10); died following a herniotomy (1); exact cause of death not known in four (4) cases in which there were quite positive statements that there had been no return of gall-bladder symptoms; nephritis (3); diabetes (3); liver cirrhosis, erysipelas, pyonephrosis, brain tumor, pernicious anemia, carcinoma of uterus (1 each); pneumonia (3).

It is a coincidence that all of the 13 patients referred to in the last paragraph which fell in the group without stones had the gall-bladder drained at operation, and of the 23 in the group with stones in the gall-bladder, in 12 the gall-bladder was drained and in 11 a cholecystectomy was performed.

Class III. Improved.—There are 63 patients listed as improved—10 per cent of the cases followed. Of these, 40 fall in the group with stones in the gall-bladder, 17 in the group without stones, and 6 in the group with stones in the common duct. In 32 of these cases, the gall-bladder was drained, and in 31 it was removed.

Table XXX shows the interval between the operation and the last reply.

TABLE XXX.

Patients improved by operation.

Interval between operation and last reply	Stones in the G. B.		Stones in the C. D.		Without stones	
	Cholecystectomy	Drainage	Cholecystectomy	Drainage	Cholecystectomy	Drainage
One month ...		1				
Six months ...	2	1			1	
One year	1	1	2		2	1
Three years ..	4	4	1		3	
Five years ...	3	4			3	1
Eight years ..	4	2			1	4
Ten years	4	6		1		
Fifteen years .		3		2		1
Total	18	22	3	3	10	7

Class IV. No Improvement or Recurrence of Symptoms.—Those patients who were not at all improved by operation and those who had a period of improvement at first but recurrence of symptoms later are placed here. It is regretted that of the 33 cases in this class, in many the time of the first recurrence of symptoms is not given. The gall-bladder was removed in 14 cases, drained in 18, and only an exploratory laparotomy performed in one case.

In the four cases in the group with stones in the common duct in which no improvement was noted, the gall-bladder had been removed. This agrees with the belief of Dr. W. J. Mayo that the gall-bladder should be removed if it alone is diseased, but drained if the whole tract is affected.

Table XXXI gives the time since operation, and the operation performed.

TABLE XXXI.

Patients unimproved by operation.

Interval between operation and last reply	Stones in G. B.		Stones in C. D.		Without stones	
	Cholecystectomy	Drainage	Cholecystectomy	Drainage	Cholecystectomy	Drainage
Six months ..	1	3	1		1	1
One year		1		1		
Three years ..	1	3	1		2	
Five years ...	2	3				
Eight years ..	1		1		1	2
Twelve years .	1	3				
Fifteen years.		2	1			
Total	6	15	4	1	4	3

Class V.—The patients dying less than one year after leaving the hospital of some trouble other than disease of the biliary tract are not included in the lists of cures or fatalities. There are 13 of these patients, 11 being in the group with stones in the gall-bladder and 2 in the group without stones. The gall-bladder was drained in 7 of these cases and removed in the remaining six.

The causes of death were carcinoma of the pancreas (2 cases); pulmonary tuberculosis and carcinoma of liver (one case of each); diaphragmatic hernia (1 case); carcinoma of stomach (2 cases); hypernephroma, pernicious anemia, pneumonia, liver abscesses, typhoid fever, cirrhosis of liver (1 case of each).

Class VI.—The nine patients in this class died more than 2 years after discharge from the hospital, and the cause of death was not given in the replies from relatives. Several replies stated that there had been no return of the pre-operative symptoms. Seven of these cases fall in the group with stones in the gall-bladder and 2 in the group with stones in the common duct. The gall-bladder was removed in 5 and drained in 4 of the cases. These cases are not included as cures or fatalities.

Class VII. No reply.—Replies as to the condition of the patients could not be obtained in 133 (18 per cent) of the

total number in the 3 groups. Of these 90 were in the group with stones in the gall-bladder, 10 in the group with stones in the common duct and 33 in the group without stones. The gall-bladder was removed in 52 per cent of these cases, drained in 44 per cent, partially removed with drainage in 2 per cent, and a choledochostomy alone performed in 2 per cent.

Summary of the Seven Classes

We shall not consider for the present the last three classes, which constitute 21 per cent of the total, because the patients were either not heard from (18 per cent) or were not classed under either cures or fatalities (3 per cent). This leaves 580 patients or 79 per cent of the entire number. All cases in which drainage of any part of the biliary tract was instituted will be considered as drainage of the gall-bladder provided a cholecystectomy was not done. This eliminates 4 cases in which only an exploratory laparotomy was done, and two in which the gall-bladder was opened and closed tightly.

In 280 cases, or 49 per cent of the remaining 574, the gall-bladder was removed, and in 294 (51 per cent) it was drained. When we analyze these cases as regards deaths, cures, improvement, and no improvement, we find: (1) Thirty-nine per cent of deaths were among patients from whom the gall-bladder had been removed and 61 among those in which it was drained. (2) In fifty-one per cent of cures, the gall-bladder was removed and in 49 per cent it was drained. (3) In forty-nine per cent of the cases improved but not cured by operation, the gall-bladder was removed and in 51 per cent it was drained. (4) As stated previously, 80 patients in the three groups underwent more than one operation. The original operation consisted in removal of the gall-bladder in 9 cases, and of drainage in 71, but four of the latter patients had the gall-bladder removed later, and subsequently an operation on the common duct. As these four patients were submitted to both operations, they will not be considered at present. Then there are 17 cases without re-operation with recurrences of symptoms following drainage of the gall-bladder and 14 following its resection. Adding these to the re-operated patients we see that of 107 patients with recurrences of preoperative symptoms without permanent improvement, only 21 per cent had had the resection of the gall-bladder while 79 per cent had had only drainage.

If we include the 4 cases in which the gall-bladder was drained first and later on was removed after which operation on the common duct became necessary, we have 13 patients who required another operation after a cholecystectomy. As stated previously, the only cases not in the group with stones in the common duct are the two in the group with stones in the gall-bladder in which a plastic operation had to be performed on the common duct because of injury at the time of removal of the gall-bladder. In 4 of the remaining 11 cases the second operation followed the first in less than 4 months, which suggests that possibly all the stones had not been removed at the first operation. The interval separating the cholecystectomy and the subsequent operation in the remaining cases is: 1 year in 3 cases; 3 years in 2 cases; 2 years in 1 case; 5 years in 1 case. Stones were found at the final operation in 10 of the 13 cases.

This series of cases is rather an ideal one for the comparison between cholecystectomy and cholecystostomy because almost the same number of each were performed. It is a little unfair to the advocates of cholecystostomy because at the present time the mortality percentage is lower for both procedures than it was previously and the gall-bladder has been removed in the greater number of cases in recent years. One might also contend that the higher mortality in the drainage series is due to the fact that the patients were often too sick at the time of operation to endure a cholecystectomy and hence the gall-bladder was drained. This may be responsible for the difference, but on reading the operative notes we find that on many of the sickest patients a cholecystectomy was performed. We have analyzed the deaths according to the operations and the condition of the patients at that time. Patients who had a majority of the following findings are classed as "bad risks:" (1) acute pain and muscle spasm, (2) elevation of temperature, (3) deep jaundice, (4) a high leucocyte count, (5) dense adhesions around the gall-bladder and (6) marked inflammation of the gall-bladder or ducts. The deaths falling in this classification include 23 of the 27 patients dying after a cholecystectomy and 33 of the 42 drained cases. This shows that, as regards the deaths after cholecystectomy, the process was in an acute stage at the time of operation in 7 per cent more of the cases than in the drainage group.

With the same point in view we shall next consider the cases in which more than one operation became necessary in this hospital, and the cases with recurrence of symptoms without re-operation. Of the 70 patients operated upon more than once, 38 had the first operation performed in the Johns Hopkins Hospital and the condition at this original operation is the one studied. Nine patients (82 per cent) of the eleven who needed a second operation following cholecystectomy were in an acute stage at the time of the first operation and 19, (70 per cent) of the 27 patients re-operated upon after cholecystostomy were in a similar condition. Of the cases with recurrence of symptoms without re-operation, we find that in 47 per cent of the cases of cholecystectomy and in 65 per cent of the drained cases, an exacerbation was in progress at the time of operation. It seems from these figures that the higher mortality following cholecystostomy cannot be explained by the poor condition of the patient at the time of operation.

Pancreatitis developed less often after removal of the gall-bladder than after drainage in this series. This

could be determined only for the patients operated upon more than once. It was present in 8 of these cases and 75 per cent followed drainage of the gall-bladder. The pancreas was described as indurated in 7 cases and in one case there was a definite abscess which had followed a drainage operation.

As has been said before, a secondary operation performed on the common duct became necessary in only 2 cases on account of injury to the common duct during removal of the gall-bladder. Both of the patients were well after a plastic operation. When the cholecystectomy is performed with care, this danger seems to be almost negligible.

When we consider that these operations were performed by a relatively small number of surgeons, all trained under very nearly the same conditions, and that the percentage of deaths and recurrences is much higher in the drained cases, whereas the percentage of well and improved patients are about the same following either operation, it would appear that cholecystectomy is the operation of choice in most cases.

Malignancy Group. Group IV.—There are 42 cases with a diagnosis of malignancy of some part of the biliary tract. Four cases with this diagnosis are not included here because it was clearly shown either by microscopic study of tissue taken or by the subsequent course that the original impression was wrong.

Etiology.—Thirty of the patients (70 per cent) were females; one patient (2 per cent) was colored.

The youngest patient with this diagnosis was 34 years old. Twelve per cent were between the ages of 30 and 40, 33 per cent between 40 and 50, 36 per cent between 50 and 60, 17 per cent between 60 and 70, and 2 per cent were more than 70 years of age. Twelve patients (30 per cent) gave a history of a preceding typhoid fever. In all but one case it antedated admission to this hospital by more than 20 years, and in this case the interval was 7 years. If stones formed in the gall-bladder in a reasonable length of time after typhoid fever, they may have played a very important part in producing the malignancy.

Twenty-three (77 per cent) of the female patients had been pregnant. There had been only one pregnancy in 2 cases, one to three pregnancies in 4 cases, three to five in 7 cases, five to ten in 7 cases, and more than ten in 3 cases.

Symptoms.—The interval separating the first symptoms suggestive of disease of the biliary tract and entrance to this hospital was: 8 days in 1 case; 2 weeks in 3 cases; 1 month in 3 cases; 3 months in 9 cases; 1 year in 7 cases; 3 years in 3 cases; 6 years in 4 cases; 10 years in 1 case; 20 years in 1 case; and 30 years in 3 cases. These figures show that 70 per cent of the patients had symptoms for less than one year preceding entry and 88 per cent had them for less than 5 years.

The first symptom suggestive of this trouble was pain in 48 per cent, indigestion in 24 per cent, jaundice in 7 per cent, malaise in 14 per cent, dark urine in 2 per cent, itching of the skin in 2 per cent, and a mass felt in the right upper quadrant in 2 per cent.

There was an interval of freedom from severe symptoms in 30 per cent of the cases, and constant symptoms in 70 per cent.

In 86 per cent of these cases there was indigestion, in 66 per cent nausea, in 65 per cent vomiting, in 81 per cent pain, in 38 per cent referred pain, in 70 per cent obstinate constipation, in 57 per cent of 37 cases, according to our notes, eructations of gas, in 78 per cent jaundice, in 50 per cent of 30 cases with notes on this point there was itching of the skin, in 61 per cent of 23 patients with notes there were chills or fever or both, in 90 per cent of 39 patients with notes there was an appreciable loss of weight, and in 2 cases, or 5 per cent, the patients thought that symptoms were brought on by taking food.

The pain is described as occupying the entire right upper quadrant in 20 per cent of cases, as limited to the epigastrium and usually to the right half in 29 per cent, as general abdominal pain in 9 per cent, as limited to the right hypochondrium in 12 per cent, as being present in the lower chest in 5 per cent, as occupying the entire upper half of the abdomen in 2 per cent. In 19 per cent there was no pain.

There was radiation of pain to the right shoulder in 7 of the 16 cases with referred pain, to the right back in 4 cases, to the left shoulder in one, to the right arm in one, to the shoulders and back in two, and to both shoulders in one case.

In 13 (31 per cent) of the 42 cases, there were attacks considered typical of biliary colic.

The histories state that jaundice had been persistent for quite a long time before entry in 55 per cent of the cases, intermittent in 21 per cent, had never been present in 21 per cent, and questionable in 3 per cent.

A comparison of the symptoms in this group with those in the groups without malignancy shows (1) the presence of symptoms for a shorter period preceding entry in this group, (2) that pain is less frequent as an initial symptom in this group by 21 per cent, (3) that the symptoms are more constant without intervals of freedom by 48 per cent, (4) a lower percentage of nausea and vomiting in this group, (5) a lower percentage of cases with pain as one of the symptoms by 15 per cent, (6) a lower percentage of referred pain by 13 per cent, (7) a higher percentage of a history of jaundice by 23 per cent, with a persistent jaundice in a much higher percentage, (8) the same percentage of itching of the skin as was present in the group with stones in the common duct, but much higher than that in the other two groups, (9) a higher percentage of loss of weight by 24 per cent, (10) a lower percentage of typical biliary colic by 50 per cent, and (11) that the

pain in this group was usually more diffuse than that in the others.

Physical Examination.—Jaundice was present on admission to the hospital in 30 of 41 cases with notes on this point (73 per cent). The liver was palpably enlarged in 71 per cent of cases and the gall-bladder palpable in 65 per cent. There was tenderness on palpation in the right upper quadrant in 68 per cent of these cases and muscle spasm in 33 per cent. Acute pain was present on entry in 19 per cent and the temperature elevated above normal in 8 of 29 cases (with notes) or 28 per cent.

Comparing these figures with those in the other groups, we find (1) a higher percentage of jaundice in this group (by thirty-four per cent) than in the three groups combined, a ratio of almost 2:1; it was 7 per cent less common in this group than in the common-duct-stone group, (2) a higher percentage of palpably enlarged livers by 49 per cent (a ratio of 3:1), (3) a higher percentage of palpable gall-bladders by 43 per cent (a ratio of 3:1), (4) a lower percentage of tenderness on palpation in the right upper quadrant, by 9 per cent, and also a lower percentage of muscle spasm in the same area, by 11 per cent, (5) the degree of fever was about the same, and the acute pain present on entry lower in this group by 12 per cent (a ratio of 5:3).

Laboratory Findings.—The stools were acholic in 10 (42 per cent) of 24 cases examined, and the urine contained bile in 20 (60 per cent) of 34 cases examined.

The white blood count was recorded in 31 of the 42 cases. In 13 (42 per cent) of these, it was below 10,000; in 10 cases (32 per cent) between 10,000 and 15,000, and in 5 cases (16 per cent) between 15,000 and 25,000, and in 3 cases (10 per cent) above 25,000. The highest leucocyte count was 39,000.

Gastric analyses are recorded in 15 cases; in 3 there was no free HCl, in 3 a very low normal, and a normal in 9 cases.

Comparing this with the other groups, we find (1) bile absent in the stools more often in this group in a ratio of 6:1, (2) bile present in the urine more often by 43 per cent, in a ratio of almost 4:1, (3) the white blood count considerably higher in this group than in the others, (4) very little difference in gastric analyses.

Operation, Re-operated Cases.—Eight of the 42 patients (19 per cent) were submitted to more than one operation. In 4 cases both operations were performed in the Johns Hopkins Hospital and in 4 cases the first operation was done elsewhere. In 7 (88 per cent) of the re-operated cases the original operation consisted in drainage of the gall-bladder, and in 1 case (12 per cent) in cholecystectomy.

The intervals between operations in the drained cases were 45 days in one, 3 months in two, six months in one, 10 months in two, 3 years in one. In the cholecystectomy case, the interval was 3 months. Stones were present in the gall-bladder in all seven of the cases with a note on the first operation.

Last Operation.—Free fluid was present in the peritoneal cavity in 13 of 41 cases (32 per cent). In 3 cases it was blood-stained, in 3 it was bile-stained, and in 7 it was clear.

Adhesions are noted in 40 cases—very numerous in 20 per cent, a few in 55 per cent, and none in 25 per cent.

Carcinomatous nodules in the liver were found in 20 cases (49 per cent); in 10 cases (24 per cent) the liver was enlarged but no carcinomatous nodules were present; in one case (2 per cent) the liver was smaller than normal, and in 10 cases (24 per cent) it was thought to be normal.

The gall-bladder is described as being quite thickened in almost every case, and in most cases as being enlarged. Stones are described as being in the gall-bladder in only 9 cases, but in most cases it was not opened, and the presence of a carcinomatous mass rendered palpation for stones quite difficult. Stones in places other than the gall-bladder were felt in the cystic duct in two cases, in the cystic, common, and hepatic ducts in one case, and free in the peritoneal cavity in one case.

The fluid contents appeared to be abnormal in all cases in which the gall-bladder was opened. There was pus in 7 cases and mucus in 3 cases.

The common duct was opened in 5 cases. A tube anchored with catgut was placed in it in three of these cases; in two cases it was closed with silk and catgut, and drains were placed down to it.

Location.—The new growth is described as carcinoma of the gall-bladder in 22 cases, of the ampulla of Vater in 1 case, of the gall-bladder and ducts in 7 cases, of all the ducts in 2 cases, of the common duct in 4 cases, of the cystic and hepatic ducts in 1 case, of the gall-bladder and cystic duct in 3 cases, of the liver and common duct in 1 case. As stated before, nodules were thought to be present in the liver in 20 cases. In one case a metastatic gland in the neck was removed and the abdomen not opened. The pancreas was thought to be carcinomatous in 6 cases.

A cholecystectomy was performed in 7 cases. In 23 cases the abdomen was drained and in the remaining 18 cases it was closed without drainage. The condition of the patient was poor at the completion of operation in many cases.

The pre-operative diagnosis was wrong in 5, doubtful in 12, and right in 25 cases.

Postoperative Notes.—So many patients died so very soon after operation that notes are of little value. In thirteen cases there was drainage of bile after operation. The incision was healed on discharge from the hospital in almost every case. Notes on bile in the urine and stool are given in very few cases. Nineteen patients died while in the hospital.

Bacteriology and Pathology.—Cultures are reported in only 4 cases. Three of these were sterile and one grew *B. proteus.*

Tissue for microscopic study was taken at operation in only 9 cases. In 7 of these the gall-bladder was removed, in one drained, and in one a metastatic gland was removed from the neck. The diagnosis was carcinoma in all of these cases.

Ultimate Results.—Of the 42 patients, 38 were followed after operation. On twenty-four of these only an exploratory laparotomy had been done. Of the 20 patients followed upon whom an exploratory laparotomy was performed, 19 were dead at the last report and the remaining one showed no improvement 5 months after operation. The time between operation and death was: 2 days in 3 cases; 5 days in 3 cases; 2 weeks in 2 cases; approximately 6 weeks in 7 cases; 6 months in 2 cases; the remaining two dying shortly after leaving the hospital.

The seven patients who were submitted to resection of the gall-bladder are dead. One lived for 2 days; 2 for 10 days; 1 for 22 days; 1 for 3 months; 1 for 7 months; and 1 for a year.

The interval between the operation and death in the 5 cases after drainage of the gall-bladder was: 8 days in 2 cases; 1 month in 1; 2 months in 1; 1 year in 1 case.

The three patients on whom a cholecystectomy was performed lived for one day, 19 days, and 6 months after operation, respectively.

One patient died in 3 months after a choledochotomy, and one in a month after the removal of a metastatic gland from the neck. The gall-bladder was opened and closed tightly in one patient who died in 2 days.

It seems that operation merely serves to hasten death, since no patient followed has lived more than a year afterwards.

Cases without Operation. Group V.—There are exactly 100 cases in this group. These patients were not operated on for one of the reasons following: (1) refused operation; (2) died before operation could be performed; (3) the condition cleared up; (4) operation inadvisable owing to the presence of some complication.

The clinical diagnoses in these cases were: (1) gall-stones in the gall-bladder, in 51 cases, (2) acute or chronic cholecystitis in 23 cases, (3) catarrhal jaundice in 9 cases, (4) carcinoma of the gall-bladder in 5 cases, (5) stones in the common duct in 12 cases.

Of these 100 patients, forty-two were males and fifty-eight females; eleven were colored; twenty-three had had a preceding typhoid fever; thirty-seven (71 per cent) of the 47 females with notes on this point had been pregnant at least once.

The figures on symptoms, physical examination, and laboratory findings will not be tabulated here, as there is such a variety of clinical diagnoses none of which were corroborated by operation.

Only 56 of these patients could be traced after leaving the hospital. Twenty-two of these were entirely well, 6 were improved, 7 unimproved, 10 had died in less than a year, and 11 after more than a year. In 8 of these 21 the cause of death was thought to be disease of the biliary tract and in most cases carcinoma.

Miscellaneous Group, Group VI. A. Pericystic Adhesions.—Eight patients had marked pericystic adhesions but the gall-bladder itself was thought to be normal otherwise.

History.—Three of these patients were males, 5 were females. The 4 females with a note on this point had been pregnant. One patient was colored. Two of the eight had had typhoid fever. The ages ranged from 28 years to 58 years, the average being 42 years.

The time elapsing since the first symptom varied between 4 months and 18 years. The first symptom was pain in five cases, indigestion in two and jaundice in one. All the patients had indigestion, 7 had nausea and vomiting, all had right upper quadrant pain, with radiation to the right shoulder in 2 cases, six had suffered from constipation, six from eructation of gas. Four patients gave a history of jaundice, constant in 1, intermittent in 3. Three patients gave a history of intervals of freedom from symptoms; in 5 they were constant. Of the 8 patients, 6 gave a history of typical biliary colic; in one the attack followed the taking of food.

Physical Examination and Laboratory Findings.—Only one patient was jaundiced on admission. Six patients had tenderness on palpation and 3 had muscle spasm. No patient had acute pain on admission.

The white blood count was not above 12,000 in any of the cases. There is nothing of interest in any of the other laboratory studies.

Operation.—There were dense adhesions in all cases. The duodenum and omentum were usually implicated along with the gall-bladder.

In one case there was an associated pancreatitis, and in 2 cases chronic appendicitis. In one case the appendix had been removed at a preceding operation.

In 6 of these cases, the adhesions were merely released and the gall-bladder was not opened. In the remaining 2 cases, in addition to release of adhesions, the gall-bladder was opened and a tube placed in it. The results following these operations were quite satisfactory.

B. Strictures of the Common and Hepatic Ducts.—There are 5 of these cases. Three of them followed removal of the gall-bladder, and in 2 cases the cause was unexplained. Of the three cases in which stricture followed injury to the common duct at operation, the description in two cases has already been given in the group having stones in the gall-bladder. In the other case, the original operation was performed elsewhere.

Both patients with strictures which did not follow a preceding operation died within two months after operation. Both were jaundiced on entry. The gall-bladder was removed in both cases, and in one a tube was placed in the common duct and in the other in the hepatic duct. One stricture was in the hepatic duct and the other in the common duct at the ampulla. A tuberculous pleurisy partly accounted for the death of one patient.

Summary

This paper represents a statistical study of all the cases with a diagnosis of disease of the biliary tract on the Surgical Service of the Johns Hopkins Hospital between 1889 and 1924. They are arbitrarily divided into groups depending on the presence or absence of stones and the position of stones when present. The cases with malignancy of the tract are considered separately. The entire number of cases are considered from the standpoints of etiology, symptoms, physical findings, laboratory findings, operations and re-operations, bacteriological and pathological studies, course immediately after operation and ultimate results.

In the cases of disease of the biliary tract treated surgically, exclusive of those with malignancy, the following are some of the more important points: (1) The average age was forty-four years the highest incidence being in the fifth decade. No cases fall in the first decade and very few in the second. The youngest patients are found in the group with disease without stones. Morbid conditions in the biliary tract are much more common in the white race than in the colored, and in females than in males. Twenty-eight per cent of the patients had had a preceding typhoid fever, the highest percentage occurring in the group without stones. Ninety-one per cent of the married women had been pregnant. (2) The most common symptom was pain; indigestion ranking next in frequency. The group with stones in the common duct had the most severe symptoms, the least severe being found in the group without stones. The shortest intervals separating the initial symptom suggestive of biliary tract trouble and the seeking of surgical aid are found in the group without stones. By far the highest percentage of persistent jaundice was found in the group with stones in the common duct. (3) Jaundice was present on physical examination in 39 per cent of all cases, the highest percentage (80) being in the group with stones in the common duct. The liver was enlarged in 22 per cent of all cases; of patients with stones in the common duct 38 per cent had enlarged livers. The gall-bladder was palpable in 22 per cent of all cases, the highest percentage being in the group with stones in the gall-bladder or cystic duct. Thirty-one per cent of these patients were in acute pain when admitted to the hospital. There was tenderness on abdominal palpation in 77 per cent and muscle spasm in 44 per cent of all cases. (4) The leucocyte counts were rather surprisingly low, in very few cases over 15,000 white cells. Twenty-three per cent of patients with gastric analyses had an achlorhydria; X-ray studies were positive for stones in 13 per cent of cases in which plates were made. (5) Fifty-eight per cent of all cultures taken at the time of operation were positive, the predominating organism being *B. coli* with *B. typhosus* ranking next. Eighty-nine per cent of all cases in which the gall-bladder was removed showed thickened walls, and round-cell infiltration was present in 98 per cent. (6) The stay in the hospital after operation was usually shorter and less disagreeable to patients after cholecystectomy than after drainage of the gall-bladder. (7) Twenty-five per cent of the patients had other pathological conditions in addition to those found in the biliary tract at the time of operation. Of these appendicitis and pancreatitis were the most common. (8) Including the patients who had had the first operation performed at another hospital, 11 per cent of the whole number required more than one operation. The gall-bladder had been drained at the original operation in 89 per cent of these cases in which another operation became necessary, the latter following in less than one year in 56 per cent of the cases and in less than five years in 86 per cent. It is interesting that in so many of the cases in which the duodenum was not probed through the common duct at the time of the original operation, surgical interference a second time was required. (9) Of the patients in these three groups, 9.5 per cent died while still in the hospital, and no reply was obtained as to their condition in 18 per cent of cases. Of the remaining 532 patients, 76 per cent were either well at the time of the last reply or until death from some other cause, 12 per cent were improved by operation, 6 per cent were unimproved, and 3 per cent had died from other trouble in less than a year after leaving the hospital. (10) This series of cases would seem almost to be an ideal for comparison between cholecystectomy and cholecystostomy, inasmuch as 49 per cent of our patients that were followed after leaving the hospital had the gall-bladder removed; and 51 per cent had it drained. The percentages of cured and improved patients following the two types of operations are about the same, but only 39 per cent of the deaths followed cholecystectomy, whereas 61 per cent followed drainage of the gall-bladder. In addition we see that 79 per cent of the patients who had recurrence of symptoms (with and without another operation) had had the gall-bladder drained at the original operation. A cholecystostomy had first been performed on 89 per cent of the patients who had to undergo a second operation. Of the patients who died following removal of the gall-bladder, 85 per cent were in an acute attack at the time of operation, while of those who died after drainage 78 per cent were in a like condition. The common duct was injured in only 2 cases in which a cholecystectomy was performed.

Forty-two cases of carcinoma of the biliary tract were studied from the same points of view, and the various findings were contrasted with those found in the groups without malignancy. The symptoms in this group were usually of shorter duration, the most prominent being pain, jaundice and indigestion. Jaundice was present on physical examination in 70 per cent of these cases. Operation merely seems to hasten death in this group, as none of the patients followed lived for more than a year.

CONCLUSIONS

The facts presented in this study would seem to justify the belief that the gall-bladder should be removed in all cases in which it is diseased, whether stones are or are not present, except in cases with malignancy of the biliary tract, provided that the condition of the patient is such that the added time under anesthesia will not lessen too greatly his chances for recovery.

In malignancy of the gall-bladder, when a positive diagnosis can be made without exploration, no operation should be performed, inasmuch as it only shortens the patient's life.

In conclusion I wish to thank Drs. Finney, Miller and Bloodgood for placing at my disposal the hospital records and for their suggestions in the writing of this paper. Miss Elizabeth Schmitz has been of great assistance in collecting the data. I wish also to thank Dr. R. G. Craig for his aid.

LIST OF TABLES

Table I. Relation of race and sex to case distribution.
Table II. Relation of age to case distribution.
Table III. Relation of typhoid fever to case distribution.
Table IV. Relation of pregnancy to case distribution.
Table V. Relation of interval between the first symptom and entry into the hospital to case distribution.
Table VI. Relation of the initial symptom to case distribution.
Table VII. Relation of various symptoms to case distribution.
Table VIII. Jaundice and its character.
Table IX. Pain and its location.
Table X. Radiation of pain.
Table XI. Location of radiation of pain.
Table XII. Findings on physical examination.
Table XIII. Laboratory findings.
Table XIV. Operators and mortality percentages.
Table XV. Free peritoneal fluid and nature of adhesions.
Table XVI. Description of gall-bladders (macroscopically).
Table XVII. Position of stones.
Table XVIII. Character of fluid in the biliary tract.
Table XIX. Types of operations.
Table XX. Treatment of cystic artery and duct.
Table XXI. Bacteriological studies.
Table XXII. Microscopic studies on gall-bladders.
Table XXIII. Time of removal of last drain.
Table XXIV. Drainage of bile after operation.
Table XXV. Condition of incision on discharge.
Table XXVI. Length of stay in hospital.
Table XXVII. Ultimate results according to arbitrary divisions.
Table XXVIII. Analysis of deaths in group with stones in the common duct.
Table XXIX. Patients well since operation with types of operations.
Table XXX. Patients improved by operation.
Table XXXI. Patients unimproved by operation.

THE EFFECT OF INTRAVENOUS INJECTION OF MERCUROCHROME ON THE KIDNEYS *

By JUSTINA H. HILL and CHARLES Y. BIDGOOD, M. D.

(From the Department of Urology of the Johns Hopkins University and the Brady Institute of the Johns Hopkins Hospital)

In the advancement of our knowledge of mercurochrome as a drug to be used intravenously, it is not only important to know that it is efficacious in certain cases of septicemia and local infections, but also, in order to place this form of therapy on a rational basis, it is necessary to determine whether there is any injury done to the vital organs of the body by its intravenous administration.

It is not uncommon, after the intravenous injection of mercurochrome, for patients to develop distressing nausea, vomiting and diarrhea, with casts and a slight amount of albumin in the urine. These symptoms and signs are transitory, and there has been no persistence of them in any of our cases. However, they denote a definite amount of gastro-intestinal and renal irritation, and it was our object in these experiments to determine its degree and duration.

In this study the kidneys were the main organs examined, as it is well known that they are especially sensitive to drugs containing mercury. To this end we injected eleven rabbits intravenously, with varying doses of mercurochrome. In the first series the following amounts were used:

Rabbit 1—1 dose 1 mg. per kilo of body-weight
Rabbit 2—1 dose 2.5 mg. per kilo of body-weight
Rabbit 3—1 dose 5 mg. per kilo of body-weight
Rabbit 4—1 dose 7.5 mg. per kilo of body-weight
Rabbit 5—1 dose 10 mg. per kilo of body-weight

* Received for publication August 1, 1924.

These animals were killed two days after injection and autopsied immediately. In none of the five were there any gross signs of mercurial poisoning. The intestines were not distended or congested in any part, and the mucous membrane nowhere showed any hemorrhage, membrane, or ulceration. The liver and spleen were normal, and also the kidneys, except for slight congestion and cloudy swelling in the rabbits which had received 5 mg. or more per kilo of body-weight. Microscopically, the kidneys were the only organs which showed any change. These slides were studied in collaboration with Dr. David M. Davis, with the following result.

RABBIT 1.—This animal received one dose of 1 mg. per kilo of body-weight, and was killed two days after injection. The glomeruli show no exudate or adhesion to Bowman's capsule. The tubules are for the most part entirely normal, excepting that in an occasional area there is slight cloudy swelling. The lumina of the tubules are patent and not dilated. All changes are slight and not generalized. This represents practically a normal kidney.

RABBIT 2.—The glomeruli in this case show very slight congestion, but there is no adhesion nor exudate within the capsule. The lumina of the tubules are normal, there being no exudate. The cells are the same as in Rabbit 1. This represents also a normal kidney, as seen in photomicrograph Fig. 1.

RABBIT 3.—The glomeruli in this kidney show slight congestion. The cells of the tubules show a slight but definite cloudy swelling which is more marked than in Rabbits 1 and 2. The nuclei show some reticulation. The lumina of the tubules are moderately dilated and in many of them there is some exudate. This shows a mild inflammatory reaction.

RABBIT 4.—The glomeruli in this kidney show slight congestion. The tubules are dilated and there is occasional exudation into the lumina. The cells of the tubules show cloudy swelling of the cytoplasm with occasional loss of the nucleus. The change here is barely distinguishable from that found in Rabbit 3, and the picture is identical with that shown in Photomicrograph Fig. 2.

RABBIT 5.—The glomeruli are normal throughout. The tubules show marked swelling of the cells which in many cases practically occludes the lumen. In other places there is definite loss of the epithelium of the tubules which amounts to an epithelial necrosis.

In comparing these kidneys it is evident that the injection of a dose up to 5 mg. per kilo of body-weight causes practically no reaction in the kidney. Five milligrams per kilo and 7.5 mg. per kilo produce a change which represents a very mild reaction. The kidney of the rabbit which received 10 mg. per kilo of body-weight showed definite injury to the kidney, so much that it would probably be dangerous to give this amount to a patient.

The second series of injections was given to determine whether or not there is any added damage done by repeated injections. Three rabbits were injected with the following amounts:

Rabbit A—12 doses of 1 mg. per kilo of body-weight
Rabbit B—12 doses of 2.5 mg. per kilo of body-weight
Rabbit C—12 doses of 5 mg. per kilo of body-weight

These injections were given twice a week over a period of six weeks, the animals being killed two days after the last injection and autopsied immediately.

Examination of the organs revealed no gross pathological lesions, and microscopically the liver, lungs, pancreas, adrenals and spleen were normal. The kidneys showed the following changes:

RABBIT A.—The glomeruli were normal. The tubules showed very slight, if any, cloudy swelling. There was no epithelial destruction or loss of nuclei. The picture here was normal, as seen in Photomicrograph Fig. 1 of the first series.

RABBIT B.—The glomeruli here were slightly congested but there were no exudates or adhesions within the capsule. The tubules show a mild degree of dilatation with slight cloudy swelling. This change is very slight, and the deviation from normal barely distinguishable.

RABBIT C.—The glomeruli here also show slight congestion. The tubules show definite cloudy swelling but no evidence of epithelial destruction. The lumina of the tubules are partially occluded because of the epithelial oedema and in some there is an exudate.

It is evident, therefore, that the changes in these rabbits are no greater in degree than in those of the first series which received a single injection of the corresponding dose.

In none of these eight rabbits has the pathological process been severe except in Rabbit 5 of the first series, which received 10 mg. per kilo of body-weight. In the remaining seven rabbits the process has been mild and has varied in direct proportion to the amount of mercurochrome given. If, therefore, the damage is not an irreparable one, it is so slight that one may be reasonably safe in giving mercurochrome intravenously in doses up to 7.5 mg. per kilo of body-weight, without fear of renal injury.

In order to determine the permanence of the renal damage we injected three rabbits with the following amounts of mercurochrome:

Rabbit I. —12 doses 1 mg. per kilo of body-weight
Rabbit II. —12 doses 2.5 mg. per kilo of body-weig
Rabbit III.—12 doses 5 mg. per kilo of body1wei

These animals were kept for two months after the last injection. They were then killed and autopsied immediately. Grossly there was no pathological change noted in any organ. Microscopically, the glomeruli were normal in all cases. The tubules in the kidney from Rabbit I which received 12 doses of 1 mg. per kilo of body-weight were entirely normal except for cloudy swelling which is not marked and which represents a minimal amount of change. The same is true of the other two rabbits of this series, the reaction being so mild that it amounts to only the slightest variation from normal, and might well be due to the ether used to cause death. There is no fibrosis or loss of renal parenchyma such as one would expect if considerable damage had been done by the injections.

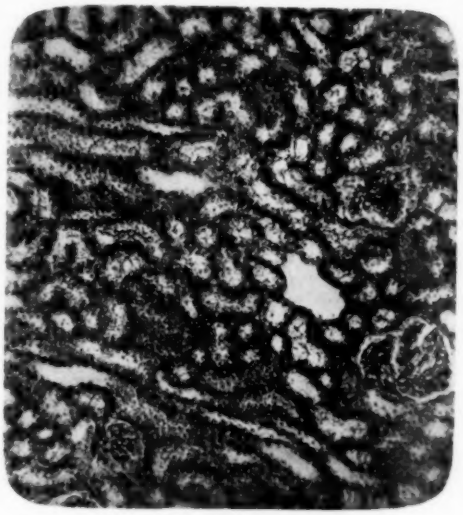


Fig. 1.
Rabbit 1.

Fig. 2.
Rabbit 2.

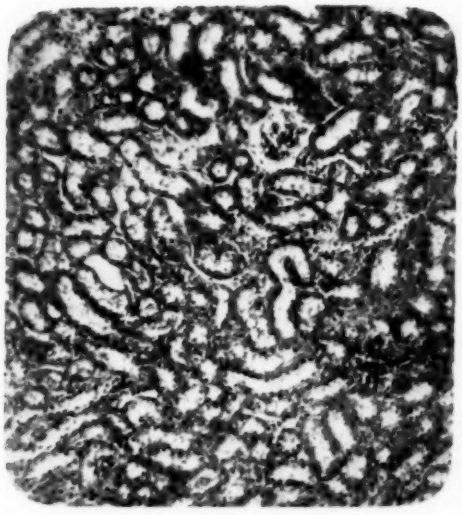


Fig. 3.
Rabbit 3.

Fig. 1.—Side-view of apparatus for determining the refractory period of the heart.

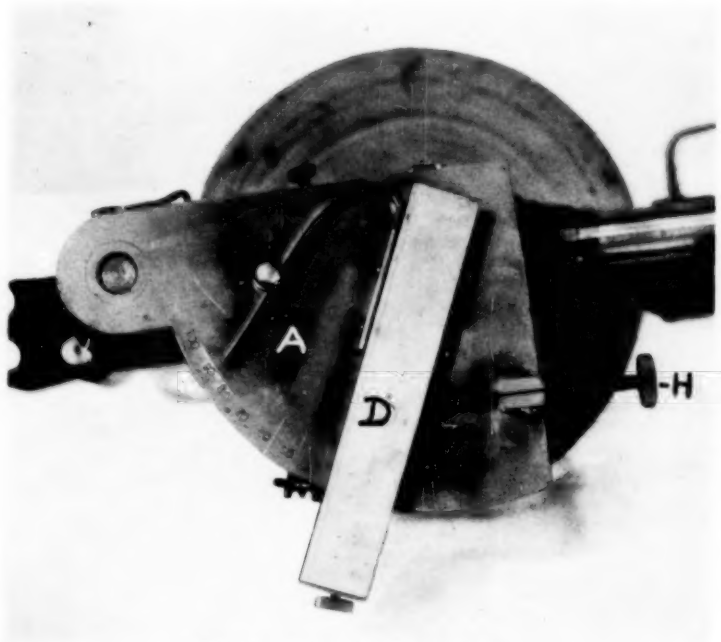


Fig. 2.—Apparatus from above.

Hence, it is safe to conclude that the retrograde changes seen in the kidneys soon after the injections do not result in permanent renal damage.

In *conclusion* it may be said that intravenous mercurochrome causes a mild reaction in the kidney which is directly proportional to the dose given. There is no actual destruction of tubular epithelium from doses as high as 7.5 mg. per kilo of body-weight, but with 10 mg. per kilo there is definite renal damage, so that it would be unwise to use so large a dose clinically.

Repeated injections do not cause any added damage, and can be given, as in these animals, as often as twice a week with safety, provided a dose of 5 mg. per kilo of body-weight be not exceeded.

The slight damage is not irreparable and at the end of two months the kidneys show no evidence of any previous lesion.

NOTE ON A TIMING DEVICE FOR THE DETERMINATION OF THE REFRACTORY PERIOD OF THE HEART *

By F. R. DIEUAIDE, M. D. and R. H. TURNER, M. D.

(From the Cardiographic Laboratory of the Johns Hopkins Hospital and University)

The apparatus to be described was devised because of the difficulty of determining the refractory period of the heart by the methods usually employed. There are two types of methods available. The first is to endeavor to interrupt the heart, while it is being driven by a suitable electrical device, by throwing in extra stimuli by hand. It is very difficult to place the extra stimuli properly without long experience, and in any case many records are wasted. The second method is to employ a continuous series of extra stimuli at a rate slightly below that at which the heart is driven. This arrangement is not sufficiently flexible for many purposes.

We have used the rotary contact maker designed by Lewis [1] and made by C. F. Palmer, of London, England, both for driving the heart and for supplying the test stimuli. The arrangement for driving remains unchanged. The machine gives only break shocks, by short-circuiting the secondary coil during the time the primary circuit is made. The apparatus devised is shown in Figures 1 and 2. A brass quadrant (Fig. 1, A) has been fastened securely to the top of the two upright posts (Fig. 1, B and C), in a horizontal position. This supports a heavy bar (D) which swings upon a rod inserted into a hole bored in a post (C) and which carries beneath the horizontal plate an additional pair of contact springs, (E and F) made just as are those for driving the heart. The contact springs are operated by hard rubber rings, each carrying a single cog (G).

The principle employed is similar to that of the automobile sparking timer. The bar (D) is held against a finely threaded screw (H) by a strong spring. The extra contacts are set at such an angle and the cogs operating them so placed that at either end of the quadrant they are operated at the same time as the driving contacts. An extra test stimulus may then be given at any chosen interval after every sixth driving stimulus by adjusting the position of D with the screw H. Since there are six cogs on the lower set of rings which operate the driving mechanism, the distance between the extreme positions of D is 60°. We have graduated this into tenths, as shown on the plate A in Fig. 2; this scale then shows the percentage of the driving interval elapsing between drive and test shocks.

The circuits used are those of Lewis (*loc. cit.*). The procedure adopted is to find the end of the refractory period roughly, by rapidly increasing the interval between driving and testing stimuli. After the neighborhood of this point is thus determined, the interrupting shocks are retarded as slowly as may be desired, by turning the screw H.

* Received for publication August 9, 1924.

BIBLIOGRAPHY

1. Lewis, T., Drury, A. N., and Bulger, H. A.: Heart, 1921, VIII, 83.

INVITATION TO AMERICAN PHYSICIANS

This Association is supervising an Inter-State Post-Graduate Clinic Tour to Canada, the British Isles and France, to start May 18, 1925. Leading teachers and clinicians of Canada and Europe will arrange and conduct clinics and demonstrations in the following cities:

Toronto and Montreal, Canada; London, Liverpool, Leeds, Manchester and Newcastle, England; Edinburgh and Glasgow, Scotland; Dublin and Belfast, Ireland; Paris, Lyon and Strasburg, France.

Besides the main tour, special tours to practically all the leading centers of Europe will be arranged. Sight-seeing trips to all places of interest in the countries visited will be included in the regular tour.

Cost of tour, including first-class hotels, board, steamship, clinic arrangements and all ordinary traveling expenses, under $1000.00.

The tour is open to physicians in good standing in their State Societies, their families and friends who are not physicians.

For information, write the Managing Director, William B. Peck, Freeport, Illinois.

THE USE OF PLASTER IN THE TREATMENT OF FRACTURED FEMURS

By W. M. Firor
(From the Department of Surgery, Johns Hopkins Hospital)

This study was undertaken in order to compare the results obtained by immediate immobilization in plaster of fractures of the shaft of the femur, with those obtained by other methods of treatment. In all there have been 102 patients treated in this hospital by reduction and immediate application of a double plaster spica. We have reviewed the case records of all the patients treated for fracture of the shaft and have endeavored to have them return for measurements and x-ray examination. All measurements have been made from the greater trochanter to the external malleolus. An effort has also been made to determine the degree of function obtained. In reviewing these cases it has been evident that they should be divided into five groups:

1. Those treated by Buck's extension.
2. Those treated by overhead extension.
3. Those treated by open reduction.
4. Those treated by *immediate* immobilization in plaster.
5. Those treated by *early* immobilization in plaster.

It is interesting to trace the transition from one method to the other. When the hospital opened in 1889 the method in vogue was Buck's extension. The demonstration of this treatment was one of Dr. W. S. Halsted's favorite exercises at Ward Rounds. It was the custom, when a patient with a recent fracture of the shaft of the femur was admitted, to measure the limb and immobilize it with sand bags. The next day, under chloroform anesthesia, the fracture would be reduced, coaptation splints applied (sometimes a coaptation plaster cast), and extension made with weights suspended over a pulley at the foot of the bed. Dr. Halsted took great pains to demonstrate to his staff the proper method of applying the bandage and of measuring the limb. To the interne fell the opportunity to verify these measurements almost daily, for only in this way could one be sure that the reduction was maintained. After ten weeks of treatment the apparatus was removed and passive motion begun; a few days later the patient was allowed the use of crutches, and four or five weeks later he was walking. When the extension apparatus was removed, it was frequently observed that the limb was stiff at the knee, that fluid was present in that joint, and that there were excoriations over the malleoli. In cases in which the reduction could not be maintained, open operation was resorted to.

In April, 1898, Dr. Harvey Cushing reduced a recent fracture of the shaft of the left femur in a patient aged 29, and maintained the reduction by a double plaster spica. After 5½ weeks the cast was removed and the result can be adjudged by the following excerpts from his note: "Absolutely no deformity, no apparent atrophy, no measured shortening, measurements confirmed, circumference of right thigh 44.5 cm., of left 43.5 cm.; no motion at seat of fracture." The use of this method was repeated four times. In the last three cases (Nos. 3, 4, 5, Table III), the results were so unsatisfactory that it was abandoned. It is only fair, however, to state that one case was complicated with a tuberculous bursitis; that in another there was delayed union (lues), and that the third history bears this note: "Cast loose, fragments slipped."

In the same year, a three-year-old patient was brought to the hospital, having fractured her femur a few hours before. With this patient, instead of extension in the horizontal direction, a bar was placed over the child's crib and pulleys and weights were attached so that vertical or overhead extension was established. This was maintained for six weeks, after which the apparatus was removed. Union was secure, and the measurements showed only 0.5 cm. shortening of the injured leg. The function was excellent. Thereafter this method was the one of choice for children.

During the years 1900 to 1915, it was customary in the fractures of adults to apply a plaster spica for two to three weeks after the extension apparatus had been removed. Gradually the casts were applied at increasingly early dates, so that in 1915 they began to be applied immediately after reduction. At first this was done only with children, but later with adults also. We have found, however, that this method does not produce satisfactory results in adults—as will be brought out subsequently. Our present method, therefore, which is designated as early immobilization with plaster, is as follows:

The patient is usually first seen in the accident room where a Thomas splint is applied; an x-ray is then taken, and the sufferer is made comfortable on the ward. If the patient is under one or two years of age, the fracture is immediately reduced (ether anesthesia), a double plaster spica applied, x-rays are taken, and the patient is kept for observation in the hospital one to two days. In patients from two to fourteen years of age, the Thomas splint is adjusted. After two or three days the patient is anesthetized, a double plaster spica applied, and if the reduction is satisfactory the patient is sent home two days later. The relatives are instructed to keep the cast clean. Every week the patient is visited by a nurse and a

member of the house staff. These visits are facilitated by the coöperation of the Social Service Department. After from seven to nine weeks the cast is removed, the patient kept in bed two weeks, measured for crutches, and these are taken to him by the social worker. If the patient is older than fourteen years, a more permanent form of intrinsic apparatus (Hodgen splint and Balkan frame) is used for three weeks. After this period a plaster spica is applied and the patient is sent home and treated there as in the preceding case. The question has been raised whether satisfactory results can be obtained by such treatment. It is in answer to this question that this study was undertaken. The following tables give the results of the five methods enumerated above:

TABLE I.

Results obtained by Buck's extension.

Service number	Age of patient	Days in hospital	MEASUREMENTS			Interval between injury and measurement
			Injured limb (cm.)	Uninjured limb (cm.)	Difference (cm.)	
738	4	46			—1.0	7½ wks.
1015	4	60			—1.5	8 wks.
1038	38	68			—2.5	7 wks.
1687	34	83			0.0	12 wks.
2362	24	50			—1.0	5 wks.
2371	26	46			—0.5	6 wks.
4552	5	41			0.0	7 wks.
5147	5	56			—0.5	4½ wks.
5912	43	48			—1.0	6½ wks.
5929	8	60	55.5	55.0	+0.5	7½ wks.
7379	24	37			—3.0	5 wks.
8285	38	49			—1.5	6½ wks.
9197	58	117	80	83	—3.0	16 wks.
9353	12	33	67	68	—1.0	4½ wks.
11097	21	48	91	91	0.0	6 wks.
11504	66	89	90	92.0	—2.0	6 wks.
12046	65	57	82	80	+2.0	7 wks.
12453	8	75	60.5	61.5	—1.0	10 wks.
13745	8	46	52	51.5	+0.5	6 wks.
14932	17	62	80.5	79	+1.5	7 wks.
16394	49	90	85	88	—3.0	8 wks.
17481	49	113	86	89	—3.0	7½ wks.
17941	22	92	85	87	—2.0	10 wks.
19537	50	56	84.7	86.7	—2.0	4½ wks.
20508	42	75	86.5	85.5	+1.0	10 wks.
21124	25	82	80		0.0	8 wks.
21387	50	78	72	75.5	—3.5	7 wks.
21952	14	54	74	75	—1.0	4½ wks.
22125	40	58	83	85.5	—2.5	7½ wks.
22688	9	56			+0.5	7½ wks.
24139	8	32	52.5	54.5	—2.0	4 wks.
24248	7	28	53	54	—1.0	13 yrs.
24929	9	34	58	57.5	+0.5	4½ wks.
25967	65	95	90.5	92.5	—2.0	6 yrs.
27781	10	34	69.5	71.0	—1.5	4 wks.
33339	10	36	89.5	89.5	0.0	10 yrs.

TABLE II.

Results obtained by overhead extension.

Service number	Age of patient	Days in hospital	MEASUREMENTS			Interval between injury and measurement (wks.)	Comment
			Injured limb (cm.)	Uninjured limb (cm.)	Difference (cm.)		
7625	3	54	35.0	34.5	+0.5	8	
9001	1½	29	*	*	—1.0	4	
12970	3	49	37.0	38.5	—1.5	5	
13369	7	32	50.0	51.0	—1.0	4	
13373	3½	52	41.5	41.5	0.0	5	
14594	4½	60	51.0	51.0	0.0	8	Knee stiff 9th wk. Slight excoriation of skin.
14784	3	48	33.0	33.0	0.0	5½	Abrasion of skin.
14839	3½	52	*	*	0.0	5	
18669	5	67	44.5	44.5	0.0	9	
20324	4	134	40.5	41.0	—0.5	12	Injured leg painful three months later. Rickets.
20607	6	51	50.5	50.5	0.0	5½	
21420	4	36	42.0	42.0	0.0	4½	Slough on dorsum of foot.
21473	2	35	32.0	32.0	0.0	4	
21778	5	51	41.0	41.0	0.0	4½	
25900	4	37	85.0	85.5	—0.5	12	
27646	8	50	56.2	56.5	—0.3	6	
28041	1	46	80.5	82.0	—1.5	12	
28512	7	39	54.3	57.0	—2.7	4	
56387	5	39	24.5	25.0	—0.5	4	
58385	7	77	54.0	55.0	—1.0	10	Wound of soft parts prevented use of plaster.

* Actual measurements not given.

TABLE III.

Results obtained after open reduction.

Service number	Age of patient	Days in hospital	Difference in measurements of limbs (cm.)	Interval between injury and measurements	Method used at operation	Comment
19509	65	111	—2.5	3½ mos.	Lane plate	
19588	58	113	—1.0	3 mos.	Wired	
22967	18	82	0.0	15 yrs.	Lane plate	Flexion of knee only 30°. Unimpaired function now 3 mos. after injury.
40735	10	25	0.0	7 yrs.	Intramedullary bone peg	
44292	12	37	0.0	5½ yrs.	Intramedullary bone peg	

TABLE III.—Continued.

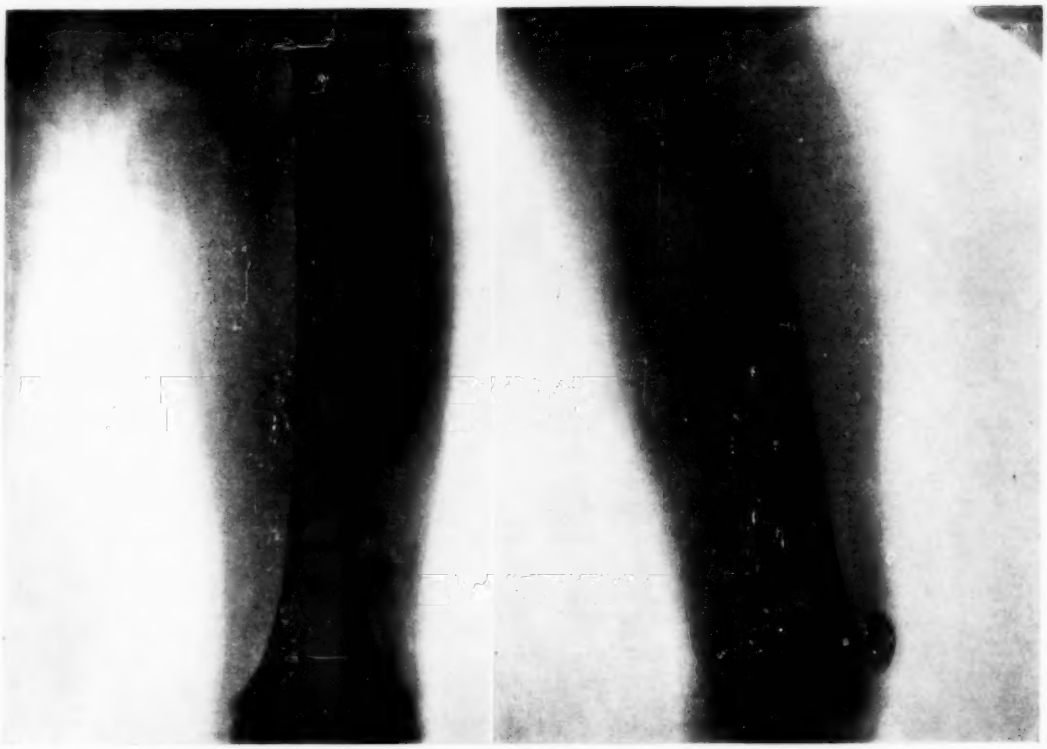
45797	5	41	0.0	5 yrs.	Wired	
48439	7	51	0.0	3¼ yrs.	Simple approximation	
48440	17	39	—1.0	3¼ yrs.	Simple approximation	Moderate bowing. Slight limp.
50395	33	20	+0.5	2½ yrs.		Slight limp. Pain on strenuous exercise.
56392	4	56	+0.5	1 yr.	Lane plate	
57539	24	73	0.0	½ yr.		Limps ½ yr. later.
57638	14	45	—2.0	1 yr.	Lane plate	Flexion of knee slightly limited; limps 1 year later.

The foregoing tables present only those cases in which accurate measurements have been made. There have been, in all, 102 patients treated in this hospital with whom immediate immobilization in plaster has been attempted. These patients are divided into three groups according to their age. Of these 102, 22 were over fourteen years of age; 27 were between seven and fourteen years, and 53 were seven years or less. The results in these three groups vary greatly. Of the 22 adult cases, only 15 were successful; of these 15 patients, seven have recently been examined and six of the seven have a shortening of 1.5 cm. or more. Of the 27 patients between seven and fourteen years, only six had to have open operation, and in the 53 of seven years or less, in only three was the method supplanted by another. There have been 24 patients in the last two groups that have returned for measurements and

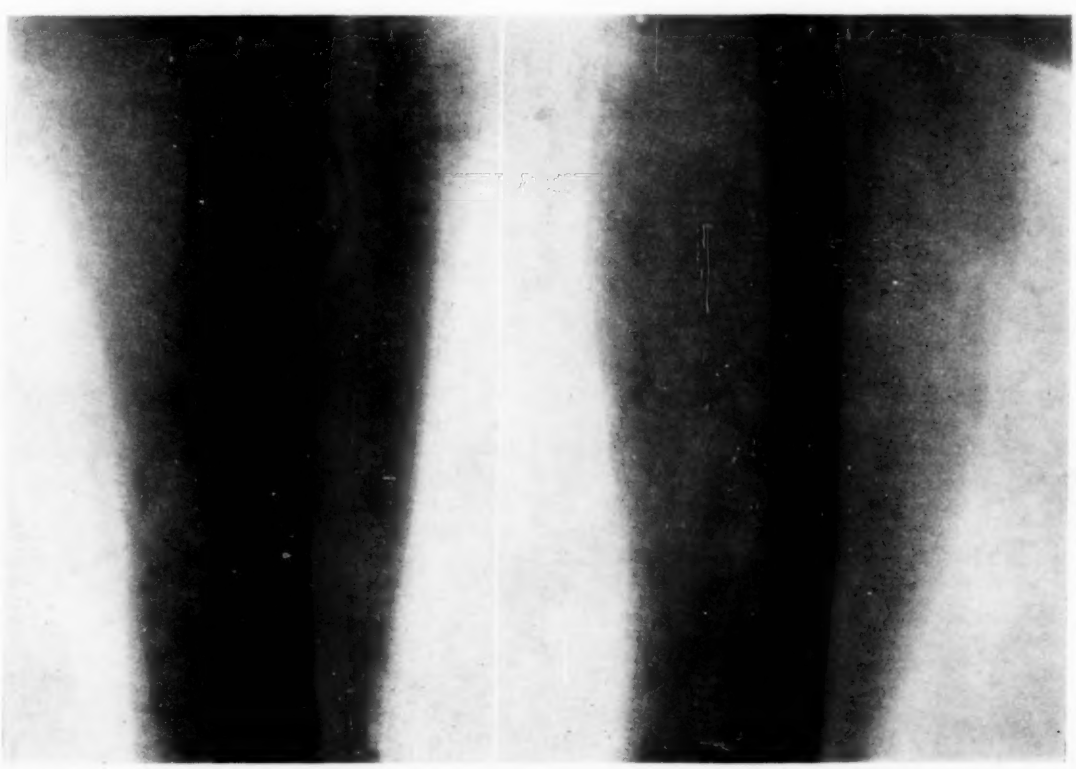
TABLE IV.

Results obtained by immobilization in plaster.

Service number	Age of patient	Days in hospital	Difference in measurements of limbs (cm.)	Interval between injury and measurements	Attempts at reduction	Comment
7649	29	58	0.0	5½ wks.	1	Seven years later no shortening; no impairment of function.
7784	29	110	—2.0	9½ wks.	1	Delayed union. Lues.
8641	53	44	—5.0	5½ wks.	1	Tbc. bursitis. Flexion of knee limited.
8723	10	42	0.0	5½ wks.	1	
9036	15	93	—4.0	3 wks.	1	Cast loose; removed in three weeks. Extension resorted to.
34940	4	3	+0.5	9 yrs.	1	Function excellent.
35096	2	13	+0.5	9 yrs.	1	
38011	52	59	—3.5	8 yrs.	1	Walks with slight limp. Patient had delirium tremens at time of reduction.
41413	16	35	—1.5	7 yrs.	1	Walks with limp. Slight anterior bowing.
42361	4	3	0.0	7 yrs.	1	
43862	9	5	+0.5	6 yrs.	1	No impairment of function, six yrs. later (see Figs. 3 and 4).
45882	7	4	+1.5	5½ yrs.	1	No impairment of function, five years later.
47603	4	3	0.0	5 yrs.	1	No impairment of function, five years later.
48234	4	4	0.0	4 yrs.	1	No impairment of function, four years later.
49840	6	43	+0.5	4 yrs.	3	Slough of skin. Streptococcus infection of throat delayed discharge from hospital.
49987	5	64	+0.5	4 yrs.	2	No explanation in history for patient's prolonged stay in hospital.
50591	25	24	—1.5	3 yrs.	1	
51184	4	12	—0.5	3 yrs.	1	
52883	11	2	0.0	2½ yrs.	1	
53181	14	12	+1.0	2 yrs.	1	
54155	12	16	0.0	1½ yrs.	2	Tibia and fibula also fractured.
57295 } 57704 }	5	3	0.0	1 yr.	2	Cast broken by patient's walking at end of sixth week. Readmitted to hospital, femur refractured and held with plaster spica. See Plate No. 1 for x-ray one year after accident.
57392	3	5	0.0	1 yr.	1	
57702	12	7	—0.5	1 yr.	1	Slight limp two months later.
57705	2	10	0.0	2 mos.	1	
57967	12	10	—0.5	4 mos.	1	
58215	6	34	—1.0	2 mos.	1	Out-of-town case; could have been discharged sooner if patient had lived near hospital.
58535	5	26	0.0	2½ mos.	1	Small slough, healed in ten days.
Disp.	1½	0	0.0	2 mos.	1	Dispensary case. Parents would not leave child in hospital.
Disp.	2	0	0.0	2 mos.	1	Dispensary case. Parents would not leave child in hospital.
Disp.	2	0	—0.5	2 mos.	1	Dispensary case. Parents would not leave child in hospital.



Figs. 1 and 2.—Antero-posterior and lateral views of femur, 1 year after *refracture*. Patient walked on limb and refractured it six weeks after injury. Reduced and cast reapplied. Total hospitalization two admissions, eight days. Plates of both femurs show similar degree of old rachitic bowing. Function perfect. Measurements show 0.5 cm. shortening.



Figs. 3 and 4.—Antero-posterior and lateral views of femur six years after injury. Patient nine years old at time of injury. No disability. No shortening.

x-ray; of these, two had a shortening of 1 cm. and one a shortening of 1.5 cm. Measurements of the circumference of the limbs was made on seven patients when the cast was removed; none had appreciable atrophy. The function of the limb in the children under fourteen has been unimpaired. Of the 71 patients under fourteen in whom this method was successful, 12 had to have more than one closed reduction and application of a cast. The results in the youngest group should be compared with those obtained by the use of overhead extension, inasmuch as both groups contain patients of the same age. There have been, in all, 23 patients on whom vertical traction was employed. In only one instance was the method abandoned. Twenty patients have been followed. Three have differences of 1 cm. and in three others differences of 1.5 cm. or 2 cm. exist. The function in these patients was restored to normal soon after the extension was ended.

Results from the use of Buck's extension show that of the 56 patients on whom this was attempted, seven had to have open operations. Of the 49 remaining patients, we have measurements on 36; 15 of these have differences of 1.5 cm. or more.

Of the 26 patients on whom open reduction was used, 13 have been followed; of these only two have differences of more than 1.5 cm. The function of the injured limbs returned more slowly in these patients than in those with closed reductions. The method designated as "early immobilization" has not yet been used in a sufficient number of adults to warrant a statistical study.

The average stay in the hospital in the different groups is as follows:

Buck's extension	65 days
Open reduction	57 days
Overhead extension	50 days
Immobilization in plaster (Early and Immediate)	19 days
a. Over 14 years	34 days
b. Between 7 and 14 years	15 days
c. Under 7 years	14 days

SUMMARY

The records of all the patients treated in the Johns Hopkins Hospital for recent fractures of the shaft of the femur have been reviewed.

There have been five methods of treatment employed for these patients: (1) Buck's extension, (2) Overhead extension, (3) Open reduction, (4) Early immobilization in plaster, (5) Immediate immobilization in plaster.

The transition from one method to the other is described.

The results obtained by the different methods of treatment are compared.

The average stay in the hospital of the patients treated by the various methods is tabulated.

The following conclusions seem warranted:

1. *Immediate* immobilization in plaster of fractures of the shaft of the femur does not give satisfactory results in patients over fourteen years of age, whereas in patients between seven and fourteen years the method gives good results, and in children under seven years, this method gives results which are as good as those obtained by overhead traction.

2. By the use of the method described as *early* immobilization in plaster, the period of residence in the hospital is greatly reduced.

THE FORMATION OF BILE PIGMENT FROM HAEMOGLOBIN IN TISSUE CULTURES *

By ARNOLD RICE RICH

(From the Department of Pathology, The Johns Hopkins University, Baltimore, Md.)

When red blood cells were added to living tissue cultures containing phagocytic cells from any tissue of mesodermal origin, the ingestion of the red cells and the gradual splitting of the haemoglobin into bile pigment and an iron-containing residue could be watched under the microscope. The bile pigment made its appearance within the living cells in the form of typical rhomboid or needle-shaped crystals of bilirubin (haematoidin), or as diffuse, bright green biliverdin. These intracellular pigments have the physical and chemical properties of bile pigment. After the ingestion of red cells there has also been observed within the phagocytic cell the formation of a pigment which does not give the Prussian blue reaction for iron and has not the characteristics of bile pigment. This pigment appears to be an intermediary stage in the transformation of haemoglobin into bile pigment. Another substance which is invisible in the unstained cell, but which becomes brilliantly blue when the reaction for iron is applied, has frequently been observed within the phagocytic cells by the side of the bile pigment.

Cultures of cells of ectodermal or endodermal origin remained indifferent to red blood cells, but the presence of phagocytic cells of mesodermal origin from any part of the body was almost invariably accompanied by the ingestion of the red cells and the intracellular conversion

* Abstract of experiments presented before the Johns Hopkins Research Society on May 28th, 1924. A more detailed report will appear later.

of their haemoglobin into bile pigment and an iron-containing residue. Tissue juices and dead tissues of different types (including dead connective-tissue phagocytes) were without effect upon red blood cells.

In a drop of blood incubated alone, the mononuclear cells of the blood often ingest the surrounding red cells and, as the haemoglobin of the ingested cells disappears, bile pigment and an iron-containing substance may appear within the mononuclear phagocyte.

It seems certain from the evidence accumulated so far that the ingestion of red blood cells by phagocytes of mesodermal origin can be followed by the conversion of the haemoglobin into bile pigment and an iron-containing residue within the body of the phagocytic cell. We have as yet obtained no evidence that cells of ectodermal or endodermal origin have this power.

These observations are contrary to the belief that haematoidin is never formed from phagocytized haemoglobin, and they support the view that the phagocytic reticuloendothelial cells may be concerned in the transformation of haemoglobin into bile pigment. Whether the phagocytic cells liberate a ferment which is able to bring about this transformation extracellularly is not yet certain, but various experimental procedures are being applied to the solution of this problem.

WILLIAM WOOD RUSSELL

When the Hopkins Hospital staff was small, and the new institution was just starting out to achieve a reputation in the thronging new fields of opportunity in medicine and surgery, the quickening spirit of a common impulse for investigation and research seemed to knit the men in the different departments more fraternally and intimately than in later years. At any rate, the men of those earlier halcyon days have ever since looked back with wistful longing whenever they recalled their quondam activities, the fresh enthusiasm and happy zeal of their co-workers and the warm friendships thus engendered.

William Wood Russell was one of the genial spirits of that early group who fully appreciated its opportunities and shared in its spiritual gifts, but, alas, like so many of the comity, he has recently left us; so it seems fit to us who knew him best and cherished him that a memento of our loss should be placed in the Hospital Bulletin.

The son of one of the founders of Minneapolis, he was born there July 29, 1866. Thirty years before, Roswell Philip, his father, at the age of sixteen, had left Vermont with two Indian guides and pushed through to Minneapolis—then St. Anthony's Falls, in mid-winter, crossing the Mississippi on a dog-sled. His marriage to Marion Bradford Patch was the first in Minneapolis, and Dr. Russell's oldest sister was the first white child born there. So surprisingly close have we been living to what has long seemed to us to be ancient history!

Desirous of a better education than the West could give him at that time, William came East to school and college and took a civil engineering course at the Pennsylvania Military Academy, Chester, Pennsylvania. Just before graduation in 1887, the prophecy of a fortune teller that a medical career awaited him seems to have touched his fancy and perhaps to have led to his matriculation in the Medical School of the University of Pennsylvania where he graduated in 1890.

He then came to us at the Johns Hopkins Hospital as an intern in gynecology, completing his internship as chief resident. With this association began a life-long friendship with the group of active men at the Hopkins which he ever cherished. In common with so many, he had an especial affection and deep admiration for Osler and Welch. In 1897, he went to Germany and met Ehrlich, studied pathology under Orth at Goettingen, and visited sundry Continental clinics. Again in Baltimore, he became my associate professor in gynecology at the Hopkins, did excellent systematic work teaching our students, and built up a large private practice in which he was warmly supported by his devoted friends, J. M. T. Finney, Henry M. Thomas, and Louis P. Hamburger. His charming personal qualities and sterling integrity, as well as his technical skill, were the important elements in the substantial success achieved. He served also on the staffs of the Hospital for the Women of Maryland and of the Union Memorial and was my most acceptable associate in my private hospital. Other close friends and zealous coworkers in gynecology on the Hopkins staff were John G. Clark of Philadelphia and Guy L. Hunner. Especially warm were the friendships of William H. Baltzell, one of Halsted's well-known early men, and "Tony" and Mrs. Anthony Shorb Murray who seemed almost members of our staff in their generous hospitality. It was Mr. Murray who did the first extensive clinical photographic work in the Hopkins Hospital and who developed in our department vertical photography of specimens and photographing under water, leaving a record of several thousand pictures of operative technique and gynecological pathology. Another intimate was G. Brown Miller now of Washington.

Dr. Russell continued in active work until 1921, when a long latent and oft threatening outbreak of an active tuberculosis forced his retirement. Leaving Baltimore, he went to Pasadena; Tucson, Arizona; and Redlands. Feeling much better, he started back East in May, 1923, by way of Colorado Springs where he died suddenly on July 11; Dr. Gerald Webb attended him in his last illness.

On April 15, 1899, he married one of my private hospital staff, Ellen Cromwell Perkins, who died in 1905, leaving two children, Roswell Philip and Elizabeth Anna.

He was one of the founders of the American College of Surgeons and was present in Chicago at the inauguration of his friend, John M. T. Finney, as its first president. He was a trustee of McDonough School.

In his earlier professional life, he published gynecological papers but, later, poor health kept him from any confining work. However, in spite of his constantly threatening health, he was the author of some thirteen articles. He made a report of "The Clinical Course of Forty-seven Cases of Carcinoma of the Uterus Subsequent to Hysterectomy" (Johns Hopkins Hospital Bulletin, 1895, VI, 154-157), noting that a recurrence is likely to take place within eighteen months. One of his best surgical ideas was abdominal hysterotomy as an exploratory measure (Supra-Pubic Hysterotomy as a Means of Diagnosis and Treatment of the Uterus—The Johns Hopkins Hospital Bulletin, 1906, XVII, 134-140; Ann. Gynec. and Pediat., 1909, XXII, 90-92). Without any doubt his most important contribution was a carefully made objective study of a case, the first reported, of endometrial tissue in the ovary, which, in view of the later studies of Thomas S. Cullen and John A. Sampson of the same staff, has proved far reaching in its consequences.

HOWARD A. KELLY.

THE ISOLATION OF ADENINE NUCLEOTIDE FROM BLOOD*

By WILLIAM S. HOFFMAN

(From the Department of Physiological Chemistry of the Johns Hopkins School of Medicine)

It is the object of this preliminary communication to announce the isolation of crystalline adenine nucleotide from pig's blood. Although the existence of the substance in blood has been indicated in the past by indirect evidence, its presence has not hitherto been demonstrated by the isolation of a pure, crystalline, analyzable substance, having the chemical composition and physical properties of adenine nucleotide.

The crude nucleotide was obtained from deproteinized pig's blood by means of its lead salt and purified by recrystallization of its crystalline brucine salt out of 35 per cent alcohol. From the pure brucine salt pure adenine nucleotide in characteristic crystalline needle clusters was prepared in the usual way through the lead salt.

The substance exhibits supersaturation to a marked degree, but finally crystallizes from hot water with one molecule of water of crystallization, which it sharply loses at 110° and takes up again quantitatively on exposure to air at ordinary temperature. It responds in minutest amount to the pentose color reactions, contains the amount of nitrogen required for crystalline adenine nucleotide, and on hydrolysis with dilute sulphuric acid produces the theoretically required amount of adenine but not a trace of guanine. In short, the chemical composition and physical properties of the substance agree in detail with those of adenine nucleotide prepared from yeast nucleic acid by Jones and Kennedy.

* Received for publication Nov. 11, 1924.

NOTES ON NEW BOOKS

Problems in Tuberculosis. By SIR JAMES KINGSTON FOWLER. 63 pp. $1.50. *(Henry Frowde and Hodder and Stoughton, London, 1923.)*

It would appear that the medical profession in England has been over-zealous in reporting tuberculosis in patients who subsequently have been found not to be tuberculous. In an effort to correct this error, the author goes to the other extreme and would restrict the diagnosis much more closely to the finding of bacilli in the sputum. Of the number of patients who in the minds of able phthisiographers deserve a "provisional" diagnosis and need the benefits of a modified tuberculosis regimen little or nothing is said. As to the source of the error of a too frequent positive diagnosis, the insufficient training of students in this branch, the dependence upon x-ray pictures and the inability of the radiographer to render a clinical diagnosis are well set forth. For the most part, however, the book concerns itself with matters of administration and organization in tuberculosis work. It is at once critical, pessimistic and stimulating. It contains some excellent suggestions as to the organization of the tuberculosis "settlement" which includes a sanatorium department, a hospital and an industries department. It gives a particularly good elaboration of the workshops and outdoor industries, although those who disbelieve in the principles of Walther and M. Peterson would dissent from some of the statements. It emphasizes the importance of the discovery of contacts. It is attractively written and its last chapter comprises the author's *obiter dicta*.

H. S. W.

Applied Pathology in Diseases of the Nose, Throat, and Ear. By JOSEPH C. BECK, M. D., F. A. C. S. $7.50. *(St. Louis, C. V. Mosby Co., 1923.)*

The conspicuous lack of an English textbook limited to the pathology of diseases of the nose, throat and ear prompted the writing of this volume. It is divided into a discussion of the acute and chronic diseases of the nose, pharynx, larynx, trachea, oesophagus and ear. The symptomatology, clinical findings, pathology and treatment of each condition are pre-

sented. Considerable attention is given to treatment. The actual pathological discussion is in many places disappointing. This is particularly true for the section devoted to chronic diseases of the ear. There are numerous excellent photographs, but many of the photomicrographs, particularly in the sections on diseases of the tonsil and larynx, are very indistinct. The book avowedly is written not as a textbook but as a record of personal experience and therefore does not attempt to present a complete discussion of every subject. While not a notable pathological contribution, it will be of interest to those who recognize the need for more careful pathological investigation of diseases of the nose, throat and ear. C. A. H.

An Introduction to the Study of the Mind. By WILLIAM A. WHITE. 116 pp. $2.00. *(Nervous and Mental Disease Publ. Co., 1924.)*

This little book is addressed to medical students, nurses, and social workers. It is written to "create a point of view," that is, to present to this special group the attitude towards psychological facts which has grown up to meet the needs of modern psychiatry. In twenty-six chapters, crowded into the space of one hundred pages, Dr. White touches on the evolution of matter and man and society, he gives to "mind" a place in the evolutionary scheme, he alludes briefly to methods of study, he plunges into definitions and illustrations of psychoanalytic terminology and the psychology of wish and conflict, and he ends with a chapter on the importance of psychological insight as a corrective for primitive and unanalyzed medical theorizing.

Obviously, this is too heavy a burden for so small a book to carry. To the initiate, it is a compilation of interesting but frequently debatable fragments; to the novice, it is feared, it is likely to seem almost incoherent. And because the need for such a volume is great, and because Dr. White is in many ways so peculiarly fitted to write it, one cannot help wishing that it had been done on a fuller scale. L. S. K.

The Circulatory Disturbances of the Extremities, including Gangrene, Vasomotor and Trophic Disorders. By LEO BUERGER, M. A., M. D. $8.50. *(Philadelphia and London, W. B. Saunders Company, 1924.)*

This is a volume which should meet with a cordial welcome and which will undoubtedly be widely used. With a single exception the field is very thoroughly dealt with. The newer work on the physiology of the capillary circulation is well represented. The chapter on intermittent claudication is particularly interesting and well done.

Needless to say, the subject of thrombo-angiitis obliterans is presented excellently, especially from the points of view of its pathology and the clinical picture. This disease, which largely owes its recognition to the author, has only slowly become widely known as a clinical entity.

It is curious that arteriovenous fistula, which has such a profound effect upon both the local and general circulation, is omitted, as recently some very fundamental work upon the subject has been published.

The division of the book, which consists of 600 pages, into 108 chapters disfigures it and tends to obscure the relations between the subjects dealt with. The bibliography is very satisfactory and the bibliographic index is a feature which deserves especial praise. Such an index would enhance the value of many a volume of the scope of the present one. The illustrations are excellent.

Doctor Buerger's book may be highly recommended. It is the only work satisfactorily covering the field from a modern view point. F. R. D.

International Clinics. Ed. by HENRY W. CATTELL, A. M., M. D. and CHARLES H. MAYO, M. D. [*et al*] Vol. 11, 34 s. $2.00. *(J. B. Lippincott Co., Philadelphia, 1924.)*

In keeping with the general plan of its previous volumes, this number of International Clinics covers in its twenty-one papers a wide range of subjects in the fields of medicine, surgery, pediatrics, pathology and therapeutics. Most of the papers are appropriately of general interest, approaching the broad aspects of a given subject in a non-technical way, but interspersed with an occasional one which is so extremely specialized as to seem almost out of place in a publication of this sort. Such banal subjects as "Acute Appendicitis," "Jaundice as a Symptom of Disease" and "Poliomyelitis" contribute little that is original to the literature but serve to bring together in an interesting way sound crystallized opinion about certain common conditions which ever deserve attention.

Among several papers on physiotherapy is an article on "Mechanical Vibration in Cardio-Vascular Conditions." In it one is confronted with such statements as this: "Apical presystolic murmurs . . . . are treated . . . . with the ball vibratode . . . . between the seventh cervical and first dorsal vertebrae. The results are usually an improved heart form . . . ., the force is strengthened, and the murmur diminished;" or " . . . . application of the static wave current over the liver to enhance activity, as the patient was toxic." There is little to choose between such obsolete concepts on the one hand, and such ultra-modern empiricism, on the other. A. R. F.

The Hygiene of Marriage. By ISABEL E. HUTTON. 6 shillings. *(London, W. Heinemann, Ltd., 1923.)*

This volume deals with the problems which men and women meet before and after they enter into the married state. The simple, dignified and very human approach to the topics is done without sacrificing the accuracy of the knowledge offered. The point of view is natural and sane and the information offered should be of considerable value in helping newly married couples to make a more satisfactory adjustment to the married state. It is a book that can be safely recommended by physicians and parents. There is a short chapter devoted to contraceptive measures. F. H. A.

Haemorrhoids. Their Actiology, Prophylaxis and Treatment by Means of Injections. By ARTHUR S. MORLEY, F. R. C. S. Eng. Late temporary assistant surgeon to St. Mark's Hospital for Cancer, Fistula and other diseases of the Rectum. $2.00. *(London, Henry Frowde; Hodder & Stoughton, The Lancet Building, 1 Bedford Street, Strand, W. C. 2.)*

This book is one of the series of Oxford Medical Publications. The text proper is 101 pages in length followed by an appendix containing a number of illustrative cases and an index which is quite satisfactory. There are nine illustrations, a number of which are copied from the well known work of Ball on the "Rectum." To Americans it may seem unusual to find a monograph written on such a comparatively limited subject as haemorrhoids and to learn further that more than half of the book is an elaborate description and argument for a particular form of treatment. Indeed the evident purpose of this publication is to champion the treatment of internal haemorrhoids by the method of injection. The first five chapters are general in character and contain a very good description of the anatomy, pathology, symptoms and diagnosis of haemorrhoids in general. They add nothing particularly new, but point out in a clear and accurate manner the facts with which every practitioner of medicine should be

familiar. It is the latter half of the book which is of especial interest. As the author himself admits, the method of injection has fallen into disrepute, particularly in America, because it was introduced and largely practiced by quacks who had no knowledge of medicine and who simply carried out a routine procedure which frequently got them into trouble because of their lack of consideration of the various factors involved. The writer makes a vigorous protest against the final judgment of the method because of its misuse in improperly trained hands. His array of facts is rather convincing. He has applied this treatment in several thousand cases and quotes statistics to show that complications and mishaps are less common than after the operative treatment. He admits, however, quite frankly that recurrence is much more frequent following treatment by injection and states that in his hands it has run as high as 16.6 per cent of all cases treated. There is a careful description of the technique employed and of the precautions to be taken. These include the limitations of the method strictly to internal, bleeding and prolapsing haemorrhoids; cases having associated fissures, polyps, external haemorrhoids, thrombosis, fistula, etc., are not considered proper for treatment by the injection method. As a larger number of haemorrhoid cases include one or more of these additional lesions it is evident that the injection method has by no means universal applicability. This limitation of the field of usefulness and the high percentage of recurrence seem to be the greatest drawback to the method under discussion.

The particular material injected by Mr. Morley is a 20 per cent solution of carbolic acid with equal parts of glycerine and water. The reviewer has used the injection method in a comparatively small number of cases and feels that it will not supplant operation as the standard method of attack in haemorrhoids, simply because many of the most troublesome cases have another lesion associated with them which requires operation, and of course if one operates for any reason it is obvious that the removal of the haemorrhoids should be included.

The book serves a useful purpose in bringing to serious consideration a method which has perhaps been condemned by prejudice without sufficient trial, but suffers from the overenthusiasm that one learns to expect when a defense of a favorite method of treatment is presented. H. B. S.

Anesthesia. By JAMES TAYLOR GWATHMY, M. D. Second Revised Edition. $6.50. *(New York and London, The Macmillan Company, 1924.)*

Dr. Gwathmy's book on Anesthesia was published in 1914 when comparatively little had been written on this subject. It has been a friend and guide to all anesthetists and students of anesthesia. As First President of the American Anesthetist's Association the author is in a position to write with knowledge and authority. One might expect a record of greater progress in the ten years which have elapsed since the first edition. Of the 750 pages, 650 remain unchanged. Four chapters have been omitted and five added. The new chapters are entitled: Third Stage Anesthesia, Synergistic Analgesia and Anesthesia with special reference to Magnesium Sulphate, Anesthesia during the World War, Ethylene Anesthesia, and Painless Childbirth by Synergistic Methods. This new material is handled clearly but rather briefly. The broad statement in Chapter XIII affirming that "an overdose of ether is any amount of that drug given over and above that which is actually necessary to produce the first stratum of the third stage" is startling in connection with the unrevised text dealing with ether anesthesia.

This volume will prove helpful and stimulating to every anesthetist. M. B.

A Synoptic Chart of Skin Diseases. By B. BURNETT HAM. $5.00. *(New York, P. B. Hoeber, 1923.)*

As indicated in the title, a synopsis is given by means of two colored charts, depicting anterior and posterior views; and a text in chart form arranged under the following titles—Name (of disease), Synonym, Description, Etiology, Common Sites, Irritation, Diagnosis (differential), Note (outstanding clinical features) and Treatment. (The parentheses include our interpretation.)

Although there is good reason to take issue with the author in some of the statements about the common diseases, it must be remembered that a work essentially didactic in character must of necessity be concise and clear. Since it serves rather as a diagrammatic guide or key, there is much to commend its usefulness. There is much which might be added to the headings under the various conditions depicted; but if such addenda were incorporated the work would at once appear too much detailed, and it would, perforce, fail in the purpose for which apparently it was presented—to give a rapid photographic survey to aid in diagnosis and in treatment.

Characteristic locations of skin diseases are in the main faithfully depicted, but to certain ones exception might be taken, viz:—urticaria pigmentosa on the thigh rather than on the body; chilblains and Raynaud's disease on the ear rather than on the fingers and toes; seborrhoea corporis in the popliteal space,—small inaccuracies which are excusable in a chart of this kind. Furthermore, the presentations of dermatitis herpetiformis and of pemphigus, of alopecia areata and of tinea tonsurans, are not sufficiently and distinctively dissimilar.

The type is very readable; the book is somewhat cumbersome and perhaps could be used more easily, if the colored charts were mounted separately and the covers were placed in such a way as to permit of ready turning of the pages. It might have been more practicable to have printed the text on one side of the paper only, and thus allowed of mounting of each page.

On the whole the presentation is decidedly a worthy addition to our hitherto inadequate methods of teaching Dermatology. I. R. P.

Goiter. Non-Surgical Types and Treatment. By ISRAEL BRAM. *(The Macmillan Company, New York, 1924.)*

There is a type of book replete with information of a certain kind that appears to answer every question of the perplexed practitioner. This volume on goiter contains an astonishing amount of material and a wide review of the literature with certain limitations. There are several matters, however, of considerable importance about which the author, it seems to us, is out of accord with the best thought of the day; for example, he feels that Graves' Disease should never be treated surgically except in the presence of pressure symptoms or carcinoma; he relegates the metabolic rate to a position of secondary importance and does not give careful records of its determination in the various types of goiter; thirdly, the author believes in the value of quinine and various other remedies in Graves' Disease, and has very little to say with regard to iodine, the one outstanding medium for medical treatment. We feel that in this book the pendulum has swung to an extreme degree away from surgical interference in Graves' Disease; whatever one's theoretical beliefs as to the etiology of this condition, he must be impressed by the occasional value of thyroidectomy in patients who are being seriously intoxicated by exophthalmic goiter. The author has a great deal on his side in his belief that Graves' Disease will usually respond eventually to medical treatment, but it is

difficult to convince an unbiased observer that an acutely ill patient should forego the immediate relief by operation in favor of a medical cure that might be years in the future. The book appeared at a rather unfortunate time, for iodine therapy in Graves' Disease, at least as a pre-operative measure, has just been shown to be worth more than all other medical procedures together; these reports from the Mayo Clinic and elsewhere make Dr. Bram's volume already somewhat out of date. The subject of endemic and sporadic goiter is exhaustively treated; there is little to be desired in this part of the volume, although one would hesitate to follow Dr. Bram's advice to induce mild intoxication with thyroid extract in the attempt to clear up certain simple goiters. J. T. K.

A Memoir of William and John Hunter. By GEORGE C. PEACHEY. *(William Brendon and Son, Ltd., Plymouth, 1924.)*

The quotation on the title page, taken from a letter of William Cullen on the death of David Hume, really gives in epitome the key to this book: "These are a few particulars which may appear trifling, but to me no particulars seem trifling that relate to so great a man."

Instead of a general view of the lives of the two great Scotsmen, William and John Hunter, an impressionistic picture, as it were, with no special regard for actual facts, a form of biography so much in vogue in recent years, Dr. Peachey confines himself to tracing in chronological order the particulars of their lives, their habitations, their work, their interests, their publications, their friends and enemies, incidents often omitted or incorrectly stated in the existing lives of these men. The amount of reading and research required to uncover these particulars is far beyond the patience of most biographers. They have been discovered by reviewing the newspapers of London and Edinburgh, from the birth of William Hunter to the death of his nephew, Matthew Baillie, and even beyond, really the reading of the newspapers of the whole 18th Century, as well as of rate books, registers of wills, records of the London Hospitals, especially those of St. George's, and indeed of many obscure sources likely to throw light on the careers of these two men or on the lives of their relatives, friends and contemporaries who exerted an influence upon them.

The result is a work of infinite value to the student of medical history. Not only is the story intensely interesting, but the reader has presented to him many new facts hitherto undiscovered and unpublished. Interesting original letters are printed for the first time and in an appendix are given the documents which led up to the final insult and sudden death of John Hunter in the waiting room of St. George's Hospital.

The book is an outgrowth of the author's previous study of the history of this hospital into which early in life he entered as a student. His interest in the hospital naturally centered in the great surgeon, which in turn carried him on to the older brother, William, and so to a study of the teaching of Anatomy before and during his lifetime, with a resulting most instructive chapter on the early teaching of the subject.

The form of the book is excellent, well printed with several interesting illustrations and a complete index—the whole, a most valuable, interesting and accurate account of the Hunter brothers. H. B. J.

BOOKS RECEIVED

The Doctor Looks at Literature. Psychological Studies of Life and Letters. By Joseph Collins. 1923. 8°. 317 pages. George H. Doran Company, New York.

Outlines of Medical Zoölogy. With Special Reference to Laboratory and Field Diagnosis. By Robert W. Hegner, William W. Cort and Francis M. Root. 1923. 12°. 175 pages. MacMillan Company, New York.

The Common Neuroses; Their Treatment by Psychotherapy. By T. A. Ross, M. D., F. R. C. P. E. 1923. 8°. 256 pages. Longmans, Green & Co., New York; Edward Arnold & Co., London.

Physiotherapy Technic. A Manual of Applied Physics. By C. M. Sampson, M. D. With eighty-five illustrations. 1923. 8°. 443 pages. C. V. Mosby Company, St. Louis.

Woman's Hospital in the State of New York. Report of the Scientific Work of the Surgical Staff. Volume IV, 1921-22. Edited by George Gray Ward, M. D., F. A. C. S. 1923. 8°. 292 pages. C. V. Mosby Company, St. Louis.

Peking Union Medical College. Contributions. Including Papers Delivered at the Dedication Ceremonies September, 1921. Volume II, 1922. 4°. Peking, China, 1923.

Walter Reed and Yellow Fever. By Howard A. Kelly, M. D. Third edition, revised. 1923. 8°. 355 pages. The Norman, Remington Company, Baltimore.

The Ophthalmic Year Book. Containing bibliographies, digests and indexes of the literature of ophthalmology for the year 1922. Volume XIX, 1923. 4°. 390 pages. Ophthalmic Publishing Company, Chicago.

A Clinical Guide to Bedside Examination. By Dr. H. Elias, Dr. N. Jagic and Dr. A. Luger. Arranged and translated by Wm. A. Brams, M. D. 1923. 12°. 135 pages. Rebman Company, New York.

Procedures in Nursing. Preliminary and Advanced. By Annabella McCrae. 1923. 12°. 261 pages. Whitcomb & Barrows, Boston.

Obstetrics for Nurses. By Charles B. Reed, M. D. One hundred and forty-four illustrations, including two color plates. 1923. 8°. 399 pages. C. V. Mosby Company, St. Louis.

Principles of Bacteriology. By Arthur A. Eisenberg, A. B., M. D. Second edition. 1923. 8°. 214 pages. C. V. Mosby Company, St. Louis.

A Text-book of Chemistry for Nurses. By Fredus N. Peters, A. M., Ph. D. Second edition. Illustrated. 1923. 8°. 302 pages. C. V. Mosby Company, St. Louis.

Surgery of the Spine and Extremities. A Text-book for Students and Practitioners. By R. Tunstall Taylor, B. A., M. D., F. A. C. S. With 604 illustrations. 1923. 8°. 550 pages. P. Blakiston's Son and Company, Philadelphia.

United States, War Department. The Medical Department of the United States Army in the World War. Volume I, The Surgeon General's Office. Prepared under the direction of Maj. Gen. M. W. Ireland, M D. By Col. Charles Lynch, M. C., Lieut. Col. Frank W. Weed, M. C., Loy McAfee, A. M., M. D. 1923. 8°. 1389 pages. Washington, Government Printing Office. Washington.

The Centennial of the University of Virginia, 1819-1921. The Proceedings of the Centenary Celebration, May 31 to June 3, 1921. 4°. 235 pages. G. P. Putnam's Sons, New York and London, 1922.

Physical Diagnosis. By Richard C. Cabot, M. D. Eighth edition, revised and enlarged, with six plates and 279 figures in the text. 1923. 8°. 536 pages. William Wood and Company, New York.

Nursery Guide for Mothers and Nurses. By Louis W. Sauer, M. A., M. D. Illustrated. 1923. 12°. 188 pages. C. V. Mosby Company, St. Louis.

Rhus Dermatitis. From Rhus Toxicodendron, Radicans and Diversiloba (Poison Ivy), its Pathology and Chemotherapy. By James B. McNair. 1923. 8°. 298 pages. University of Chicago Press, Chicago, Illinois.

INDEX TO VOLUME XXXV OF THE JOHNS HOPKINS HOSPITAL BULLETIN

Abdominal distention, post-operative, The use of eserin and strychnin in, 370.

Abel, J. J., Physiological, chemical and clinical studies on pituitary principles, 305.

Adenine nucleotide, The isolation of, from blood, 417.

Adrenal insufficiency and atrophy of the cortex following venous obstruction of the suprarenal glands, 54.

Adrenals and the chromaffin system, Experimental observations on the, 187.

Amoss, H. L., and Ford, F. R., Results of the injection of encephalitic spinal fluid into rabbits, 20.

Anastomotic circulation in the dog, An experimental study of the, 385.

Anemia, pernicious, An analysis of the clinical histories of patients with, in the Johns Hopkins Hospital from 1918 to 1922 inclusive, 38.

Arsenic Dermatitis in a child, treated with sodium thiosulphate, 78.

Arthritis, Chronic, in the adult, associated with splenomegaly and leucopenia. A report of five cases of an unusual clinical syndrome, 16.

Arthritis, Syphilitic, with eosinophilia: recovery of *T. pallidum* from the synovial fluid, 235.

Bacilli of Vincent, spirochaetae and fusiform, Pulmonary infection with the, 368.

Barrera, F de P., and Chavarria, A. P., The acute exanthem of leprosy, 147.

Beck, C. S., A study of lymph pressure, 206.

Bidgood, C. Y., and Hill, J. H., The effect of intravenous injection of mercurochrome on the kidneys, 409.

Bile pigment, The formation of, from haemoglobin in tissue cultures, 415.

Biliary tract disease, A statistical study of eight hundred and eighty-eight cases of, 391.

Bilirubin, Experiments on the extrahepatic formation of, 158.

Blalock, A., A statistical study of eight hundred and eighty-eight cases of biliary tract disease, 391.

Blood-chemistry and blood-volume, Changes in, following reduction of renal substance, 168.

Blood-chemistry during pregnancy, 133.

Blood grouping, Further studies on. I. The antigenic properties of two types of "Group II" erythrocytes, 23.

Blood grouping, Further studies on. II. The influence of temperature upon isohaemagglutination, 33.

Blood grouping, Further studies on. III. The varied types of "Group IV" blood, 81.

Blood grouping, Further studies on. IV. The demonstration of two additional isoagglutinins (D and Q) in human blood, 126.

Blood grouping, Further studies on. V. The recognition of three types of "Group II" blood, 221.

Blood-pressure, A preliminary study of the, following reduction of renal substance with a note on simultaneous changes in blood-chemistry and blood-volume, 168.

Blood pressure, elevation in, Further observations on the, produced by guanidine compounds, 186.

Blood pressure, The effect of methyl guanidine on the, 140.

Blood serum, An experimental study of ununited fractures with especial reference to the inorganic bone-forming elements in the, 378.

Blood-volume, simultaneous changes in blood-chemistry and, A preliminary study of the blood-pressure following reduction of renal substance with a note on, 168.

Bloomfield, A. L., and Felty, A. R., On the mode of transmission of the streptococci associated with tonsillitis, 115.

Bogert, L. J., and Plass, E. D., Plasma protein variations in normal and toxemic pregnancies, 361.

Books received: 163; 262; 337; 381; 420.

Bowden, D. T., and Huck, J. G., On the peculiar morphology of a malarial parasite in a case of chronic malaria in the temperate zone, 122.

Bugg, C. R., and Folkoff, C., Arsenic dermatitis in a child, treated with sodium thiosulphate, 78.

Burky, E. L., and Smith, D. T., Impetigo contagiosa in children —its etiology and treatment, 78.

Carcinoma of the breast, Marked structural alteration in a, recurring after eleven years, 52.

Cash, J. R., A preliminary study of the blood-pressure following reduction of renal substance with a note on simultaneous changes in blood-chemistry and blood-volume, 168.

Chavarria, A. P., and Barrera, F de P., The acute exanthem of leprosy, 147.

Chesney, A. M., Kemp, J. E., Resnik, W. H., Syphilitic arthritis with eosinophilia: recovery of *T. pallidum* from the synovial fluid, 235.

Chloroform poisoning, A chemical study of a case of, 46.

Chromaffin system, Experimental observations on the adrenals and the, 187.

Clapp, C. A., The mechanism in the production of increased tension in hydrophthalmos, 85.

Clasmatocytes, Hofbauer cells, of the human chorionic villus, 183.

Clough, P. W., The protective power of normal human serum against pneumococcus infection, 328.

Cortex, Atrophy of the, Adrenal insufficiency and, following venous obstruction of the suprarenal glands, 54.

Creadick, A. N., and Stander, H. J., Blood volume in pregnancy, 1.

Crowe, S. J., and Wislocki, G. B., Experimental observations on the adrenals and the chromaffin system, 187.

Cunningham, R. S., The effects of chronic irritations on the morphology of the peritoneal mesothelium, 111.

Cutler, M., A clinical study of hypernephroma, 214.

Cysts, Diffuse uterine gland, in a cat, 49.

Davison, W. C., Rich, A. R., and Greene, C. H., Xeroderma pigmentosum. A clinical and pathological report of one case, 285.

DeGaris, C. F., Notes on some interrelations of fibroblasts in tissue culture, 90.

Dermatitis, Arsenic, in a child, treated with sodium thiosulphate, 76.

Diabetes Mellitus, On the use of intarvin fat, glyceryl margarate, in, 265.

Dieuaide, F. R., Observations on the respiratory gases in ventricular paroxysmal tachycardia, 229.

Dieuaide, F. R., and Turner, R. H., Note on a timing device for the determination of the refractory period of the heart, 411.

Diabetic patients, Glycerin, its use as an antiketogenic substance in the diet of, 201.

Duncan, E. E., Stander, H. J., and Moses, B. L., The excretion rate of urea in the toxemias of pregnancy, 97.

Eclampsia and allied conditions, Non-protein nitrogen retention during, The blood nitrogen curve in normal and in toxemic pregnancies, 345.

Elman, R., and Rothman, P., Adrenal insufficiency and atrophy of the cortex following venous obstruction of the suprarenal glands, 54.
Elvers, C. F., A new apparatus for heating bacterial and blood smears, 94.
Encephalitic spinal fluid, Results of the injection of, into rabbits, 20.
Eosinophilia, Syphilitic arthritis with, recovery of *T. pallidum* from the synovial fluid, 235.
Erythrocytes, The antigenic properties of two types of "Group II," 23.
Eserin, The use of, and strychnin in post-operative abdominal distention, 370.
Evans, F. A., and Willson, C. R., An analysis of the clinical histories of patients with pernicious anemia in the Johns Hopkins Hospital from 1918 to 1922, inclusive, 38.
Fallopian tubes, Spontaneous peristalsis of the excised whole uterus and, of the sow with reference to the ovulation cycle, 246.
Felty, A. R., and Bloomfield, A. L., On the mode of transmission of the streptococci associated with tonsillitis, 115.
Felty, A. R., Chronic arthritis in the adult, associated with splenomegaly and leucopenia, 16.
Felty, A. R., and Keefer, C. S., Acute disseminated lupus erythematosus. Report of three fatal cases, 294.
Femurs, fractured, The use of plaster in the treatment of, 412.
Fibroblasts in tissue culture, Notes on some interrelations of, 90.
Firor, W. M., The use of plaster in the treatment of fractured femurs, 412.
Firor, W. M., and Ford, F. R., Gliomatosis of the leptomeninges, 108.
Firor, W. M., and Ford, F. R., Primary "sarcomatosis" of the leptomeninges, 65.
Fistula, arteriovenous, Congenital. An embryological study, with the report of a case, 271.
Folkoff, C., and Bugg, C. R., Arsenic dermatitis in a child, treated with sodium thiosulphate, 76.
Ford, F. R., and Amoss, H. L., Results of the injection of encephalitic spinal fluid into rabbits, 20.
Ford, F. R., and Firor, W. M., Gliomatosis of the leptomeninges, 108.
Ford, F. R., and Firor, W. M., Primary "sarcomatosis" of the leptomeninges, 65.
Fractures, ununited, An experimental study of, with especial reference to the inorganic bone-forming elements in the blood-serum, 378.
Germanium dioxide, and of sodium germanate, A comparison of the effects of, on the blood of the albino rat, 180.
Glands, suprarenal, Adrenal insufficiency and atrophy of the cortex following venous obstruction of the, 54.
Gliomatosis of the leptomeninges, 108.
Glycerin, its use as an antiketogenic substance in the diet of diabetic patients, 201.
Glyceryl margarate, in diabetes mellitus, 265.
Greene, C. H., Rich, A. R., Davison, W. C., Xeroderma pigmentosum. A clinical and pathological report of one case, 285.
Guanidine compounds, Further observations on the elevation in blood pressure produced by, 186.
Guthrie, C. G., and Huck, J. G., Further studies on blood grouping. I. Antigenic properties of two types of "Group II" erythrocytes, 23.
Guthrie, C. G., and Pessel, J. F., Further studies on blood grouping. II. The influence of temperature upon isohaemagglutination, 33.
Guthrie, C. G., and Pessel, J. F., Further studies on blood grouping. III. The varied types of "Group IV" blood, 81.
Guthrie, C. G., and Pessel, J. F., Further studies on blood grouping. IV. The demonstration of two additional isoagglutinins (D and Q) in human blood, 126.
Guthrie, C. G., Pessel, J. F., and Huck, J. G., Further Studies on blood grouping. V. The recognition of three types of "Group II" blood, 221.
Guttmacher, A. F., and Wislocki, G. B., Spontaneous peristalsis of the excised whole uterus and Fallopian tubes of the sow with reference to the ovulation cycle, 246.
Guttmacher, A. F., Diffuse uterine gland cysts in a cat, 49.
Haden, R. L., and Orr, T. G., Melanuria in the absence of melanotic tumor, 58.
Haemoglobin in tissue cultures, The formation of bile pigment from, 415.
Hanrahan, E. M., Jr., Marked structural alteration in a breast carcinoma recurring after eleven years, 52.
Harris, J. W., The after-effects of the late toxemias of pregnancy, 103.
Heart, left auricle of the, Rheumatic lesions of the, 327.
Heart, refractory period of the, Note on a timing device for the determination of the, 411.
Heart block, complete, in chick embryos during the second, third and fourth days of incubation, The demonstration of, I. Studies on the physiological anatomy of the embryonic heart, 87.
Hill, E. C., Notes on an opaque X-ray mass, 218.
Hill, J. H., and Bidgood, C. Y., The effect of intravenous injection of mercurochrome on the kidneys, 409.
Hofbauer cells (clasmatocytes) of the human chorionic villus, 183.
Hoffman, William, The isolation of adenine nucleotide from the blood, 417.
Hohman, L. B., The treatment of post-encephalitic Parkinson syndrome with hyoscin hydrobromide, 333.
Huck, J. G., and Bowden, D. T., On the peculiar morphology of a malarial parasite in a case of chronic malaria in the temperate zone, 122.
Huck, J. G., and Guthrie, C. G., Further studies on blood grouping. I. The antigenic properties of two types of "Group II" erythrocytes, 23.
Huck, J. G., Guthrie, C. G. and Pessel, J. F., Further studies on blood grouping. V. The recognition of three types of "Group II" blood, 221.
Hughson, W., Meningeal relations of the hypophysis cerebri, 232.
Hughson, W., and Scarff, J. E., The influence of intravenous sodium chloride on intestinal absorption and peristalsis, 197.
Hydrophthalmos, The mechanism in the production of increased tension in, 85.
Hypernephroma, A clinical study of, 214.
Hypophysis cerebri, Meningeal relations of the, 232.
Impetigo contagiosa in children, 78.
Intarvin fat, glyceryl margarate, in diabetes mellitus, 265.
Infection (abscess), retroperitoneal and perinephritic, Cure of a, by intravenous injection of mercurochrome, 14.
Isohaemagglutination, The influence of temperature upon, 33.
Johnstone, P. N., Studies on the physiological anatomy of the embryonic heart. I. The demonstration of complete heart block in chick embryos during the second, third and fourth days of incubation, 87.
Keefer, C. S., Report of a case of Malta fever originating in Baltimore, Maryland, 6.
Keefer, C. S., and Felty, A. R., Acute disseminated lupus erythematosus. Report of three fatal cases, 294.

Keefer, C. S., Perlzweig, W. A., and McCann, W. S., On the use of intarvin fat—glyceryl margarate—in diabetes mellitus, 265.

Kelly, H. A., William Wood Russell, 416.

Kemp, J. E., Chesney, A. M., and Resnik, W. H., Syphilitic arthritis with eosinophilia: recovery of *T. pallidum* from the synovial fluid, 235.

Kidneys, The effect of intravenous injection of mercurochrome on the, 409.

Langworthy, O. R., Problems of tongue innervation: Course of proprioceptive nerve fibers; autonomic innervation of skeletal musculature, 239.

Leprosy, The acute exanthem of, 147.

Leptomeninges, Gliomatosis of the, 108.

Leptomeninges, Primary "sarcomatosis" of the, 65.

Lewis, W. H., Hofbauer cells (clasmatocytes) of the human chorionic villus, 183.

Lewis, W. H., The influence of temperature on the rhythm of the isolated heart of the young chick embryo, 252.

Lupus erythematosus, Acute disseminated. Report of three fatal cases, 294.

Lymph pressure, A study of, 206.

McCann, W. S., Keefer, C. S., and Perlzweig, W. A., On the use of intarvin fat—glyceryl margarate—in diabetes mellitus, 265.

McNeill, C., Pulmonary infection with the spirochaetae and fusiform bacilli of Vincent, 368.

MacCallum, W. G., Rheumatic lesions of the left auricle of the heart, 327.

Major, R. H., Pernicious anemia and renal insufficiency, 390.

Major, R. H., Xanthoma diabeticorum, 27.

Major, R. H., and Stephenson, W., Further observations on the elevation in blood pressure produced by guanidine compounds, 186.

Major, R. H., and Stephenson, W., The effect of methyl guanidine on the blood pressure, 140.

Malaria, chronic, in the temperate zone, On the peculiar morphology of a malarial parasite in a case of, 122.

Malta fever, Report of a case of, originating in Baltimore, Maryland, 6.

Martzloff, K. H., The use of eserin and strychnin in post-operative abdominal distention, 370.

Melanuria in the absence of melanotic tumor, 58.

Menstrual cycle and pregnancy, Changes in the human oviduct during the, 141.

Mercurochrome, intravenous injection of, Cure of a retroperitoneal and perinephritic infection (abscess) by, 14.

Mercurochrome, on the kidneys, The effect of intravenous injection of, 409.

Mesothelium, peritoneal, The effects of chronic irritations on the morphology of the, 111.

Methyl guanidine, The effect of, on the blood pressure, 140.

Moses, B. L., Stander, H. J., and Duncan, E. E., The excretion rate of urea in the toxemias of pregnancy, 97.

Nerve fibers, proprioceptive, Course of; autonomic innervation of skeletal musculature, 239.

New books, Notes on: 32; 63; 95; [illegible]; 160; 193; 226; 263; 339; 382; 417.

Nowrey, J. E., A comparison of the effects of germanium dioxide and of sodium germanate on the blood of the albino rat, 180.

Oppenheimer, E. H., Experiments on the extrahepatic formation of bilirubin, 158.

Orr, T. G., and Haden, R. L., Melanuria in the absence of melanotic tumor, 58.

Ovulation cycle, Spontaneous peristalsis of the excised whole uterus and Fallopian tubes of the sow with reference to the, 246.

Owen, T., A case of polycythaemia vera with special reference to the familial features and treatment with phenylhydrazine, 258.

Parkinson syndrome, post-encephalitic, The treatment of, with hyoscin hydrobromide, 333.

Peristalsis, The influence of intravenous sodium chloride on intestinal absorption and, 197.

Perlzweig, W. A., Keefer, C. S., and McCann, W. S., On the use of intarvin fat—glyceryl margarate—in diabetes mellitus, 265.

Pernicious anemia and renal insufficiency, 390.

Pessel, J. F., Guthrie, C. G., and Huck, J. G., Further studies on blood grouping. V. The recognition of three types of "Group II" blood, 221.

Pessel, J. F., and Guthrie, C. G., Further studies on blood grouping. II. The influence of temperature upon isohaemagglutination, 33.

Pessel, J. F., and Guthrie, C. G., Further studies on blood grouping. III. The varied types of "Group IV" blood, 81.

Pessel, J. F., and Guthrie, C. G., Further studies on blood grouping. IV. The demonstration of two additional isoagglutinins (D and Q) in human blood, 126.

Petersen, H. A., An experimental study of ununited fractures with especial reference to the inorganic bone-forming elements in the blood serum, 378.

Phenylhydrazine, A case of polycythaemia vera with special reference to the familial features and treatment with, 258.

Physicians, Invitation to American, 411.

Pituitary principles, Physiological, chemical and clinical studies on, 305.

Plasma protein variations in normal and toxemic pregnancies, 361.

Plass, E. D., Non-protein nitrogen retention during eclampsia and allied conditions. The blood nitrogen curve in normal and in toxemic pregnancies, 345.

Plass, E., and Bogert, L. J., Plasma protein variations in normal and toxemic pregnancies, 361.

Pneumococcus infection, The protective power of normal human serum against, 328.

Polycythaemia vera, A case of, with special reference to the familial features and treatment with phenylhydrazine, 258.

Pregnancies, Blood nitrogen curve in normal and toxemic, 345.

Pregnancies, Plasma protein variations in normal and toxemic, 361.

Pregnancy, Blood volume in, 1.

Pregnancy, Changes in the human oviduct during the menstrual cycle and, 141.

Pregnancy, After-effects of the late toxemias of, 103.

Pregnancy, Blood chemistry during, 133.

Pregnancy, Excretion rate of urea in the toxemias of, 97.

Pulmonary infection with the spirochaetae and fusiform bacilli of Vincent, 368.

Reichert, F. L., An experimental study of the anastomotic circulation in the dog, 385.

Renal insufficiency, Pernicious anemia and, 390.

Resnik, W. H., Chesney, A. M., and Kemp, J. E., Syphilitic arthritis with eosinophilia: recovery of *T. pallidum* from the synovial fluid, 235.

Respiratory gases, Observations on the, in ventricular paroxysmal tachycardia, 229.

Rheumatic lesions of the left auricle of the heart, 327.

Rich, A. R., The formation of bile pigment from haemoglobin in tissue cultures, 415.

Rich, A. R., Davison, W. C., and Greene, C. H., Xeroderma pigmentosum. A clinical and pathological report of one case, 285.
Rickety bones *in vitro*, The healing of, 304.
Rienhoff, W. F., Congenital arteriovenous fistula. An embryological study, with the report of a case, 271.
Rivers, T. M., and Tillett, W. S., Atypical distribution of varicella lesions dependent upon a coexistent syphilitic infection, 137.
Rothman, P., and Elman, R., Adrenal insufficiency and atrophy of the cortex following venous obstruction of the suprarenal glands, 54.
Russell, William Wood, 416.
"Sarcomatosis," primary, of the leptomeninges, 65.
Scarff, J. E., and Hughson, W., The influence of intravenous sodium chloride on intestinal absorption and peristalsis, 197.
Sex, mixed, Preliminary report of a case of. An apparent male, with a testis in scrotum on right side; ovary, tube and uterus in inguinal canal on left side, 165.
Shipley, P. G., The healing of rickety bones *in vitro*, 304.
Smears, bacterial and blood, A new apparatus for heating, 94.
Smith, D. T., and Burky, E. L., Impetigo contagiosa in children —its etiology and treatment, 78.
Snyder, F. F., Changes in the human oviduct during the menstrual cycle and pregnancy, 141.
Sodium chloride, intravenous, The influence of, on intestinal absorption and peristalsis, 197.
Sodium germanate, A comparison of the effects of germanium dioxide and of, on the blood of the albino rat, 180.
Splenomegaly and leucopenia, Chronic arthritis in the adult, associated with, 16.
Stander, H. J., A chemical study of a case of chloroform poisoning, 46.
Stander, H. J., and Creadick, A. N., Blood volume in pregnancy, 1.
Stander, H. J., Duncan, E. E., and Moses, B. L., The excretion rate of urea in the toxemias of pregnancy, 97.
Stander, H. J., The blood chemistry during pregnancy, 133.
Stephenson, W. and Major, R. H., Effect of methyl guanidine on the blood pressure, 140.
Stephenson, W. and Major, R. H., Further observations on the elevation in blood pressure produced by guanidine compounds, 186.
Streptococci associated with tonsillitis, On the mode of transmission of the, 115.
Strychnin in post-operative abdominal distention, The use of eserin and, 370.
Synovial fluid, Recovery of *T. pallidum* from the, in syphilitic arthritis with eosinophilia, 235.
Syphilitic infection, Atypical distribution of varicella lesions dependent upon a coexistent, 137.
Tachycardia, ventricular paroxysmal, Observations on the respiratory gases in, 229.
Thiosulphate, sodium, A case of arsenic dermatitis in a child, treated with, 76.
Thomas, H. M., Jr., Glycerin, its use as an antiketogenic substance in the diet of diabetic patients, 201.
Tillett, W. S., and Rivers, T. M., Atypical distribution of varicella lesions dependent upon a coexistent syphilitic infection, 137.
Tongue innervation, Problems of: course of proprioceptive nerve fibers; autonomic innervation of skeletal musculature, 239.
Tonsillitis, On the mode of transmission of the streptococci associated with, 115.
T. pallidum, Recovery of, from the synovial fluid in syphilitic arthritis with eosinophilia, 235.
Tumor, melanotic, Melanuria in the absence of, 58.
Turner, R. H., and Dieuaide, F. R., Note on a timing device for the determination of the refractory period of the heart, 411.
Urea, The excretion rate of, in the toxemias of pregnancy, 97.
Uterine gland cysts, diffuse, in a cat, 49.
Uterus, excised whole, Spontaneous peristalsis of the, and Fallopian tubes of the sow with reference to the ovulation cycle, 246.
Varicella lesions, Atypical distribution of, dependent upon a coexistent syphilitic infection, 137.
Venous obstruction of the suprarenal glands, Adrenal insufficiency and atrophy of the cortex following, 54.
Willson, C. R., and Evans, F. A., An analysis of the clinical histories of patients with pernicious anemia in the Johns Hopkins Hospital from 1918 to 1922, inclusive, 38.
Wislocki, G. B., and Crowe, S. J., Experimental observations on the adrenals and the chromaffin system, 187.
Wislocki, G. B., and Guttmacher, A. F., Spontaneous peristalsis of the excised whole uterus and Fallopian tubes of the sow with reference to the ovulation cycle, 246.
Xanthoma diabeticorum, 27.
Xeroderma pigmentosum. A clinical and pathological report of one case, 285.
X-ray mass, Notes on an opaque, 218.
Young, H. H., Cure of a retroperitoneal and perinephritic infection (abscess) by intravenous injection of mercurochrome, 14.
Young, H. H., Preliminary report of a case of mixed sex. An apparent male, with a testis in scrotum on right side; ovary, tube and uterus in inguinal canal on left side, 165.

THE JOHNS HOPKINS HOSPITAL BULLETIN

The Hospital Bulletin contains details of hospital and dispensary practice, abstracts of papers read before the Medical Society of the Hospital, reports of lectures, and other matters of general interest in connection with the work of the Hospital. It is issued monthly. Volume XXXV is in progress.

ANNOUNCEMENT OF EDITORIAL AND OTHER CHANGES

To our Subscribers:

In view of the fact that from the beginning the *Bulletin* has been published at a considerable annual loss, it has been felt that the Hospital should no longer be called upon to bear this undivided burden. For this and other reasons, the following changes will be inaugurated with the New Year, 1925.

Control of the *Bulletin* will pass to the Medical School, and an editorial board, chosen from among members of the faculty, will have charge of its publication.

The *Bulletin* will be published by the Williams and Wilkins Company, Mt. Royal and Guilford Avenues, Baltimore, Md. Subscriptions and correspondence relating to all business details should be sent direct to the publishers.

The *Bulletin* will continue to appear monthly, but instead of one volume each year, there will be two, beginning with January and July, respectively. It will be sold by the volume only. The price of each volume will be $3.00, with 50c additional for postage for countries outside the postal union.

The typographical dress will be somewhat altered, the size of the pages will be reduced to 7x10 inches but the number correspondingly increased, so that the actual amount of material published will not be lessened.

It will be the endeavor of the present Board to maintain in every way the *Bulletin's* present high standard of excellence. Reports of clinical and research work from the clinics and laboratories of the Hopkins, as well as other papers of interest, will be welcomed.

It is our hope that the new regime will not only retain all the old subscribers and friends of the *Bulletin*, but will also win many new ones. We bespeak your cooperation in making our endeavors successful.

EDWARD P. CARTER
WILBURT C. DAVISON
ARNOLD R. RICH
FRANK R. SMITH
GEORGE B. WISLOCKI